Not a Slave to the Rhythm:

The Perceptual Consequences of Rhythmic Visual Stimulation

by

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Abstract

We investigated whether rhythmic visual stimulation leads to changes in visual perception attributable to the entrainment of endogenous alpha-band oscillations. First, we report evidence that the attentional blink phenomenon is not selectively modified by alpha-band rhythmic entrainment. Next, we provide evidence that changes in single target identification following rhythmic stimulation are poorly explained by rhythmic entrainment, but well explained by alternative factors. We report failures to replicate the results of two previous visual entrainment studies supporting the hypothesis that alpha-band rhythmic stimulation leads to matching rhythmic fluctuations in target detection. Finally, we examined whether temporal acuity during an RSVP sequence is dependent on rhythmic entrainment by studying the role of object change on temporal acuity, finding novel results inconsistent with the predictions of the rhythmic entrainment model. We conclude that visual perception is robust against entrainment to task-irrelevant rhythmic visual inputs and that endogenous and externally driven oscillations in the visual system may be functionally distinct.

Dedication

For my family

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Author Notes

The current work was designed, conducted, analysed and interpreted by myself, with the generous advice of my advisors and collaborators to which I am indebted. Much of the work of Chapter 2 was designed based on previous, unpublished work, and as such these collaborators receive full credit, as noted in the text. The whole manuscript is written in first-person plural to acknowledge the input of my colleagues, though the analysis and opinions expressed are entirely my own and do not necessarily represent the views of my advisors or collaborators.

Chapter 1: Introduction

Is our brain a slave to external rhythms? A number of empirical studies and review articles have come out in recent years in support of the hypothesis that rapid, rhythmic visual and electrical stimulation produces matching rhythms in the brain, leading to psychological and perceptual changes matching those produced by endogenous oscillations. This hypothesis has broad implications in the field of neuroscience and clinical psychology and has inspired a number of alternative medicine and self-help techniques outside the mainstream scientific community. However, this hypothesis remains supported by limited evidence and is predicated on a number of critical assumptions. A better understanding of the relationship between external rhythmic stimulation and behavioural outcomes will lead to a better understanding of the brain and its relationship to the environment, and is critical for informing potential clinical treatments of disorders associated with changes in endogenous brain oscillations.

Basic Principles of Brain Oscillations

There are some generally agreed upon principles for oscillations in the human brain. Oscillations in the brain vary across an extremely broad range from the daily circadian sleep/wake cycle (~0.000012 Hz) to greater than 100 Hz firing rate of neurons in auditory pathways of the brainstem. Frequency generally varies inversely as a function of the spatial scale upon which the oscillation is maintained. This relationship makes perfect sense when considering the physical structural limitations of the brain as a physical entity and as a small world network. Neurons which are closest together tend to have the strongest interconnection, taking advantage of short conduction times for synaptic communication. Thus, ultra-fast oscillations (> 80 Hz) are typically confined to networks for a few

thousands neurons, whereas slow delta (0.5-3Hz), theta (3-8 Hz) and alpha (8-12 Hz) rhythms can be effectively synchronized regionally across cerebral cortex over several cycles. The relationship between frequency and the spatial scale of coherence leads to a characteristic of regional brain measurements by which the power of an oscillation decreases directly as a function of its frequency; a 1/f distribution. This 1/f distribution can be largely attributed to the more focal nature of faster oscillations and the nature of waveform summation: focal oscillatory waveforms at different phases will partially cancel each other out when summed over a region. However, a prominent exception to the "1/f Rule" rule is dominance of alpha-band frequency of ~10 Hz over large regions of the occipital and parietal lobes, disproportionately synchronized compared to surrounding frequencies.

The fastest relevant oscillation in the human brain is the action potential, or "firing", of a single neuron. A typical pyramidal neuron maintains a negative voltage (hyperpolarization) between the cell body and the extracellular fluid by actively transporting positively changed Na+ and Ca+ ions out of the cell body and negatively charged Cl- ions into the cell body. This "default" state of a negative charge is altered by inputs from other cells and other changes in the extracellular fluid. The extent to which the cell body remains depolarized is largely dependent on the excitatory and inhibitory inputs the cell receives from synapses formed at the dendrites of the neuron. When excitatory neurotransmitter, such as glutamate, comes in contact with ligand-gated ion channels at the synapse, the channels open and allow the influx of positive ions into the post-synaptic (receiving) cell, partially reducing the polarization of the of the cell, making more likely to fire. Conversely, inhibitory neurotransmitters, such as gamma-aminobutyric acid (GABA), open negative ion channels in the post-synaptic cell, increasing polarization reducing a cells likelihood of firing. If the post-synaptic cell reaches a critical threshold of positivity, voltage sensitive Na+ or Ca+ channels in the cells axon open, resulting in an action potential, a rapid positive depolarization along the axon of the neuron resulting in the release of neurotransmitters from the axon terminals in the synapse connecting the pre-synaptic (sending) cell to the post-synaptic cell. The pre-synaptic cell quickly shifts to a hyperpolarized state by closing Na+ channels and opening K+ channels, resulting in the efflux of K+

and hyperpolarization of the cell, preventing the cell from firing again for a brief refractory period. This rapid, bi-polar all-or-none firing sequence constitutes the primary means of transmission of information between neurons, and is typically completed less than 10 ms.

Slower and more sustained oscillations occur due to the interconnectivity of populations of neurons. Many network oscillations in the human brain, in particular gamma (30-80 Hz) oscillations, involve the concerted activity of coupled populations of inhibitory interneurons. Many interneurons are connected directly electrically via gap junctions, dramatically increasing the likelihood of simultaneous firing between neighbouring cells. Complex interconnectivity GABA interneurons with each other and principal excitatory pyramidal cells can lead to temporal windows of pyramidal activity counter-phase to the activity of the local interneuron cluster (Bartos, Vida, & Jonas, 2007). This precise rhythmic timing of pyramidal activity can greatly enhance the efficiency of communication between separate local circuits through synchronous spike timing (Womelsdorf et al., 2007), a process known as “communication through neural coherence” (Fries, 2005). As inhibitory interneuron populations can be triggered and phase-locked by a single neuronal input (Miles, 1990), functional phase-locking can occur between distant cortical sites, even at gamma frequencies (Traub, Whittington, Stanford, & Jefferys, 1996). However, most cross-regional phasic coupling is thought to be mediated by slower frequencies which in turn modulates gamma activity (Engel, Gerloff, Hilgetag, & Nolte, 2013; Liebe, Hoerzer, Logothetis, & Rainer, 2012; Sauseng, Griesmayr, Freunberger, & Klimesch, 2010), to allow for the longer windows of integration required for sustained long range coupling. The exact frequency and direction of coupling in the human brain depends on the region and task.

Measurement of Oscillations: from individual neurons to the human scalp

Oscillations in the brain can be measured with numerous techniques, reflecting the multiple scales in which they occur and the species from which the oscillations are measured. The patch clamp technique, in which a pipette is placed against the cell membrane wall of an individual neuron and a piece of the neuron is sucked through the pipette via negative pressure, allowing for an electrically isolated measurement of the intracellular space. This technique is particular useful for slice preparations *in vitro*, allowing for the measurement of individual neurons in isolation or in the presence of small networks. Experimental alternation of the voltage or chemical content in the intra or extra-cellular fluid can test specific hypotheses about the causal effects of such properties on individual neurons, to better understand the building blocks of oscillatory networks. *In vivo,* thin wire voltage-sensitive electrodes can be inserted into the extracellular fluid to measure the firing of individual and nearby neurons. When the electrode tip is place sufficiently far from any individual neuron, a low-pass filter allow for the measurement of the local field potential (LFP), the much slower fluctuation in voltage present in the extracellular fluid, primarily modulated by excitatory post-synaptic potentials (EPSPs) and inhibitory post-synaptic potentials (IPSPs); graded excitatory and inhibitory signals sent from pre-synaptic cells. When four wires are inserted in a "tetrode" formation, both the LFP and the separate firing of about 20 individual units in the network can be inferred simultaneously, providing a powerful tool for connecting spike timing in relation to input phase and frequency. Multi-contact laminar electrodes can measure through multiple layers of cortex, while multi-electrode arrays provide information from numerous nearby populations simultaneously. Two-photon microscopy can be used to view and measure hundreds of neurons simultaneously in deeper cortical layers, and information about the structure of each individual cell can be visualized. Voltage sensitive dyes can be used to visualize metabolic activity of a thousands of neurons over a small (typically <1mm) segment of the cortical surface. All of the aforementioned techniques have excellent spatial and temporal resolution measuring small areas of the brain and are routinely used in the study of neural activity in animals, though, as they require the opening of the scalp and other invasive procedures, they are rarely or never available for use with human

participants. While depth electrodes are occasionally used to find the locus of abnormal subcortical activity, the most common invasive neuroimaging technique available for use in humans is the electrocorticogram (ECOG), in which a few dozen easy-to-remove electrodes are placed ~1 cm apart are placed on the surface of the cortex, usually covering large portions of one or two cortical lobes. This technique has the advantage of measuring multiple cortical regions with excellent signal-to-noise, though the placement of electrodes is determined by clinical rather than scientific concerns, and experimental access to patients can be limited. Nearly all non-invasive neuroimaging of oscillations in humans is conducted using either magnetoencephalography (MEG) or Electroencephalography (EEG). MEG measures minute magnetic activity produced tangentially by electrical flow produced by at least tens of thousands of neurons, primarily from sources on or near the cortical surface. With the high density arrays used in the technique and further analytical processing, the MEG signal can potentially provide a spatial resolution of less than 1 cm^2 across the entire brain. The downside is that MEG equipment is very expensive to own and maintain, and radial sources from cortical gyri and subcortical sources are only weakly represented. EEG is the most widely used technique for the study of oscillations in the human brain. EEG measures voltage directly at the scalp, a summation of the post-synaptic activity of millions of neurons. Since the EEG signal depends on volume conduction and summation passing through the brain, pia mater, cerebrospinal fluid, skull and scalp, the spatial information derived from any given montage on the scalp is smooth, and an absolute determination of the source of a give signal is unknowable. However, using either high-density montages and advanced post-processing techniques or combination with techniques with high spatial resolution, an estimate of the source of coherent neural source with high signal-to-noise can be inferred to < 1cm.

Alpha Oscillations: Discovery and Physiology

The measurement of oscillations in the brain offered the first direct connection between mental activity and the activity of the human brain, and it all started with a very misguided hypothesis. A German clinical physiologist named Hans Berger, hypothesized that brains were capable of long distance telepathic communication and, inspired by the work of Richard Canton, sought to test this hypothesis by measuring electrical signals from the human brain and scalp. Using a galvanometer, Berger performed the first internationally recognized electroencephalogram experiments, disproving the viability of electrical signalling as a means of telepathy, yet nevertheless discovering the a prominent rhythmic electrical activity in the human brain distinctly related to mental state, which he dubbed the "alpha wave" (Berger, 1929; Millett, 2001). The alpha wave had a frequency of approximately 10 Hz, and varied in amplitude in response to visual and physical stimulation, different levels of arousal and general mental effort. In 1934, Adrian and Mathews (Adrian & Matthews, 1934) successfully replicated Berger's work and brought it to international prominence. They also conducted further experiments in order to characterize the nature of the rhythm. Adrian and Mathews conclude that the alpha rhythm "shows what happens in an area of cortex which has nothing to do, and it disappears as soon as the area resumes its normal work." Since then, this singular "rhythm" has been shown to be composed of a number of rhythms throughout the brain at or surrounding 10 Hz, though most share this characteristic of greatest amplitude in the absence of regionally relevant activation. In terms of nomenclature, the alpha rhythm is now often reserved for describing the rhythms believed to be generated by "visual" areas, whereas similar rhythms in the 8-14 Hz range over motor cortex (mu) and auditory cortex (tau) also respond primarily with desynchronization during to motor and auditory tasks, respectively. Even with this distinction, alpha activity can be sourced differentially from large areas of cortex spanning the occipital and parietal lobes (Chiu et al., 2012), each with distinct sensitivities in response to task demands. However, the reported pattern is generally consistent for each of these localized oscillations; with posterior occipital alpha desynchronized in response to a variety of visual inputs, while 10 Hz activity in the parietal lobe is sensitive to shifts in saccade planning (Medendorp et al., 2007), visual spatial

attention (Sauseng et al., 2005), the maintenance of items in working memory (Sauseng et al., 2009), auditory spatial attention (Banerjee, Snyder, Molholm, & Foxe, 2011; Kerlin, Shahin, & Miller, 2010), and auditory working memory (Kaiser, Heidegger, Wibral, Altmann, & Lutzenberger, 2007). Alpha-band desynchronization is also observed in frontal regions during sematic processing (Klimesch, Doppelmayr, Pachinger, & Ripper, 1997). Thus, the brain could be conceived as containing a number of ~10 Hz "idling" rhythms (Pfurtscheller, Stancák, & Neuper, 1996), the disruption of which serves as a marker for regional cortical activity.

How cortical alpha oscillations are produced and maintained remains a mystery that has been aggressively pursued only recently. The consensus through the 1960's was that the cortical alpha was determined by pacemakers in the thalamus. However, in a series of experiments starting in the 1970s, Lopes Da Silva and colleagues demonstrated in vitro and in vivo that alpha oscillations can be produced on the basis of intrinsic membrane properties in deeper layers of cortex in the absence of a cortical pacemaker (Lopes da Silva, van Lierop, Schrijer, & van Leeuwen, 1973). Lopes da Silva and colleagues also point out that the seemly random, stochastic nature of the alpha signature measured at the scalp was inconsistent with a stationary driving signal such as produced in the thalamus (Lopes Da Silva, Pijn, Velis, & Nijssen, 1997). This intrinsic oscillatory property of neocortex has been since replicated in a number of species (Connors & Amitai, 1997). Recent data paints a more complex picture, in which thalamocortical connections from the LGN to layer 4 of striate cortex (V1) provide a pacing signal (Bollimunta, Mo, Schroeder, & Ding, 2011), balanced by partially locally produced feedback connections originating from layer 6, with layer 5 serving as the primary local pacemaking source for higher level visual regions V2 and V4 (Bollimunta, Chen, Schroeder, & Ding, 2008). V4 activity is likely partially coordinated by the pulvinar, particularly during the maintenance of visual spatial attention (Saalmann, Pinsk, Wang, Li, & Kastner, 2012). A recent MEG study reports a resting-state coupling between the phase of thalamic alpha activity and the power of parietal gamma activity at a delay of ~15 ms, consistent with previous neurophysiology and a pacemaking role for the thalamus in the parietal lobe (Roux, Wibral, Singer, Aru, & Uhlhaas, 2013). The earliest "source"

pacemaker may be by high-threshold bursting thalamocortical neurons in the LGN, though the complex interconnectivity with LGN interneurons, thalamic relay-mode neurons, and corticothalamic inputs leads to a large degree or circularity when inferring cause and effect (Lorincz, Kékesi, Juhász, Crunelli, & Hughes, 2009; Vijayan & Kopell, 2012). However, there are also significant oscillatory feedback connections from early visual areas to the LGN (Bastos et al., 2014), putting to question whether an "origin" of oscillatory activity is an appropriate concept. This issue of circularity is only partially addressed by techniques such as Granger causality(Bastos et al., 2014; Saalmann et al., 2012), as hidden sources can cause spurious findings and the magnitude of the directional relationship between areas is difficult to infer from the typically low coherence values.

Regardless of the source of alpha activity, the outcome in the brain is the presence of intermittent large, broadly synchronized 8-12 Hz fluctuations in field potential over large regions of neocortex. Increased magnitude of these oscillations correspond with decreased pyramidal firing rate(Haegens, Nácher, Luna, Romo, & Jensen, 2011). The phase of alpha activity is also associated with changes with local multi-unit firing rate (Bollimunta et al., 2011; Haegens et al., 2011), with the greatest phase dependency at low firing rates and large alpha amplitudes. Alpha phase is also associated with the power of cortical gamma activity (Osipova, Hermes, & Jensen, 2008). In the macaque, the phase of alpha activity in layer 4, likely reflecting top-down thalamocortical activity is associated with changes in alpha power in the superficial cortical layers (Eelke Spaak, Bonnefond, Maier, Leopold, & Jensen, 2012). This phase dependent inhibition is likely driven by direct synaptic connections with GABA inputs, though recent evidence suggests that fluctuations in the local field potential itself may be sufficient to bias the oscillatory properties of a local neural population, blurring the line between LFP as a measure of network activity and LFP as the cause (Fröhlich & McCormick, 2010; Jones, Pinto, Kaper, & Kopell, 2000). Inhibitory inputs from thalamocortical circuits, pulsing at a rate of ~10 Hz, may lead to phasic inhibition of local processing. Functionally, this phasic inhibition leads to brief periods about every 100ms in which processing is not suppressed and local communication can occur, serving to "window" of information processing (Jensen & Mazaheri, 2010; Klimesch, Sauseng,

& Hanslmayr, 2007; Mazaheri & Jensen, 2010). Behaviourally, this hypothesis is supported by evidence that timing of a stimulus onset in relation to the phase of alpha activity as measured at the scalp with EEG is associated with the success or failure of near-threshold and masked target detection (Busch, Dubois, & VanRullen, 2009; Hanslmayr et al., 2007; Mathewson, Gratton, Fabiani, Beck, & Ro, 2009). However, the practical relevance of these windows of relative excitability remains to be tested.

Functional Role of Alpha Oscillations

A functional role for the phasic segmentation properties of alpha-band oscillations in information processing, as opposed to pure inhibition, has received a resurgence of interest in recent years (Klimesch, 2012; Palva & Palva, 2007). It has long been proposed that alpha activity could serve to provide temporal windows in which visual and cross modal information is integrated into discrete events (Samaha, Postle, Samaha, & Postle, 2015; VanRullen & Koch, 2003) with the strongest evidence supporting a role of alpha activity in audio-visual integration (Cecere, Rees, & Romei, 2014; Kerlin & Shapiro, 2015; Kristofferson, 1967; VanRullen & Koch, 2003). Under the binding-through-coherence hypothesis, cross-regional coherence of alpha activity could serve to facilitate the binding and exchange of information between distal brain regions (Doesburg, Emberson, Rahi, Cameron, & Ward, 2008; Engel et al., 2013; Fries, 2005; Palva & Palva, 2012; Varela, Lachaux, Rodriguez, & Martinerie, 2001), with the frequency of such communication reflecting properties of the cross-regional network (Cohen, 2011). Indeed, there is evidence linking that cross regional alpha coherence to auditory influences on visual perception (van Driel, Knapen, van Es, & Cohen, 2014) and visual selective attention (Saalmann et al., 2012). However, the alpha-band activity associated with functional cross-regional communication is not necessarily mechanistically the same as the broad, high amplitude, broadly synchronized alpha associated with inhibition (Palva & Palva, 2011).

The magnitude of alpha activity, particularly over sensory regions, can be considered to reflect two distinct cognitive states: externally oriented and internally oriented (Hanslmayr, Gross, Klimesch, & Shapiro, 2011). Under this theory, high alpha over visual areas occurs during an internally oriented state, when additional sensory inputs are inhibited to prevent interference with the higher-level cognitive manipulation of information already contained in short-term or long term memory. In contrast, alpha activity is suppressed during an externally oriented state, such as during visual search, as each incoming sensory input is processed to the fullest possible extent to acquire accurate representations of external objects. Sensory brain regions will naturally drift between low and high alpha states, leading to periods of enhanced or suppressed external perception, respectively. This conjecture is supported by inverse correlations between pre-stimulus alpha activity and target detection, which occur even in the absence of changes in sensory context or instruction (Hanslmayr et al., 2007; Mathewson et al., 2009). However, the direction of causality is very difficult to infer. Is the increase in alpha a marker of an increase in overall inhibition determined top-down from another region? Or is an increase in 8-12 Hz fluctuations in a sensory region sufficient to cause inhibition and therefore an internally oriented state? An obvious experimental approach to this question is to add an 8-12 Hz oscillatory rhythm directly and selectively to the sensory region of interest. If alpha activity is the cause of changes in perceptual state, then the magnitude and phase of such artificially induced oscillations should produce the same behavioural outcomes on perception as the endogenous rhythms; a decrease in perceptual detection and identification with increasing magnitude, with a more modest fluctuation in perception dependent on the phase of the induced oscillation. This external manipulation of a biological rhythm is most common referred to as entrainment.

Oscillatory Entrainment

Oscillatory entrainment is the alignment of a biological oscillation to external rhythmic input. One form of brain entrainment is sensory entrainment, the alignment internal brain rhythms with signals transduced through the senses such as vision, touch and sound. For instance, the circadian rhythm in the suprachiasmatic nucleus naturally oscillates in an ~24 hour cycle, the phase of which is entrained by the light emitted by the rising and setting of the sun, resulting in periods of sleep and wakefulness matching night and day (Czeisler, Weitzman, Moore-Ede, Zimmerman, & Knauer, 1980). This form of entrainment operates over a wide range of frequencies, from periods of a month to a few milliseconds (Akhoun et al., 2008; McClintock, 1971). Entrainment in the brain can easily be achieved by photic driving, the rhythmic presentation of visual input at rates up to 100 Hz (Adrian & Matthews, 1934; Herrmann, 2001) and rhythmic auditory stimulation at rates up to 1000 Hz (Akhoun et al., 2008; Henry & Obleser, 2012). The brain frequencies produced by sensory driven entrainment often match the frequency of the sensory input (fundamental frequency, *f*), though the phase alignment of the harmonics of the entrainment frequency are often reported, and can be particularly strong at double the fundamental frequency (2^{nd} harmonic, 2*f*) (Adrian & Matthews, 1934; Gomez-Ramirez et al., 2011). The level of entrainment achieved can be measured as the magnitude of power at the entraining frequency and its harmonics, as well as by measuring the phase coherence between the entraining signal and the neural response. The most common method of measuring brain response to sensory entrainment is the steady-state response (SSR) in EEG recordings in humans, though sensory driven entrainment has been confirmed through measurements of both LFP and multi-unit activity (MUA) in animal models (Lakatos, Karmos, Mehta, Ulbert, & Schroeder, 2008). The causal determinants of sensory entrainment are nearly as complex as that of endogenous oscillations, particularly when the input signal is a series of discrete events. Models of the relationship between rhythmic inputs and oscillations could be placed in three broad categories: phase alignment, resonance, and superposition.

The phase alignment model of oscillatory entrainment requires the existence of an endogenous rhythm which is maintained in the absence of external stimulation. Each time a relevant input event

occurs, the phase of the on-going oscillation is partially or entirely shifted to align with the input, without a substantial change in the magnitude of the endogenous signal. The circadian rhythm is an excellent example of entrainment by phase alignment, as the sleep-wake cycle occurs indefinitely at a roughly daily interval even in the absence of any exposure to sunlight, and the shift to a new solar rhythm can be gradual over several days as demonstrated by the phenomenon of jet lag. Resonance occurs when an external input matches the preferred oscillatory frequency of a system, producing a larger, frequency-matched response. Stimulation at a resonant frequency can lead to a substantial, non-linear change in the amplitude of an endogenous oscillation, or trigger an oscillation that is not initially present. For instance, pushing a pendulum can start a pendulum swinging, though only pushes timed with its natural swing frequency will make it swing higher. Superposition is the independent linear addition of multiple waveforms. Waveforms of many physical systems sum linearly, leading to highly predictable outcomes. If each subsequent external input produces the same response, then the summed waveform will combine constructively or destructively to determine the summed outcome. Noise-cancelling headphones work in accordance with this principle, emitting a signal 180 degrees out-of-phase with the unwanted noise, summing the sound wave to zero resulting in the absence of the targeted sound at the ear. Even in the absence of band-limited resonance in a system, superposition can often produce increases in the measured amplitude at the frequency of stimulation and harmonic frequencies. These broad categories of entrainment are not mutually exclusive, but rather can occur simultaneously and, in the case of phase alignment and resonance, interactively.

These models are relatively easy to experimentally distinguish when the natural endogenous signal is largely stationary, at fixed amplitude and frequency, and from single oscillatory source. Unfortunately, none of these assumptions generally hold when measuring endogenous alpha activity in the brain. Despite being one of the most stationary oscillations in cortex, unlike a pendulum, the phase and amplitude of the alpha rhythm is often highly unpredictable beyond a few cycles. This instability in alpha phase and amplitude can be due to a number of factors including internal

resetting events, frequency shifts, reductions of amplitude in noise, and the presence of overlapping signals. It has been proposed that visual stimulation leads to a partial phase-realignment of ongoing endogenous oscillations, as alpha power may remain constant following stimulation while phase becomes locked to the onset of the stimulus (Makeig et al., 2002). However, it has been countered that the phase of oscillatory alpha measured at the scalp is insufficiently stationary to distinguish between a phase realignment to endogenous oscillations and the superposition of an evoked response, and that the absence of a change in alpha power is insufficient to rule out the superposition of an oscillation independent evoked response (Goldstein, 1970; Mazaheri & Jensen, 2006). Sauseng and colleagues laid out several experimental predictions under the phase realignment which would point to the validity of this model, though these predictions have only been substantiated in piecemeal throughout the literature (Sauseng et al., 2007). Thus, both practically and mathematically, superposition and realignment cannot be entirely distinguished if such signals emanate from overlapping sources, particularly when measured at the scalp, and both likely contribute to any externally affected cortical signal. The situation is further complicated by the fact that the most prominent outcome of natural visual stimulation is generally a dramatic *reduction* in globally synchronized alpha activity.

Imaging Measures of Alpha-Band Entrainment

The measurement of EEG and MEG steady-state response in response to alpha-band visual stimulation has led to mixed results and interpretations with regards to the nature of occipital alpha entrainment. Until recently, research into neural alpha-band activity has assumed that the response at 10 Hz was non-linear and therefore could be attributed to a resonant response in visual cortex (Adrian & Matthews, 1934; Herrmann, 2001). However, Capilla and colleagues thoroughly investigated this claim by measuring the EEG response to checkerboards counter-phasing at a

number of frequencies, including 10 Hz, with and without jittering the exact temporal position of each counter-phase (Capilla, Pazo-Alvarez, Darriba, Campo, & Gross, 2011). When the average rate of stimulus change was held constant, no differences in the evoked potentials between jittered and non-jittered streams were observed, except as entirely predicted by the summation modal. Furthermore, rhythmic and arrhythmic both led to activity stimulation which persisted for less than 3 cycles and again were best explained as a final transient response, as would be produced by a single item. Although two subsequent studies have reported greater phase-locking for regular vs irregular alpha band rapid serial presentation, neither study could rule out transient superposition as the cause, as the significant difference phase locking in both studies was small and was at most a few cycles (Mathewson et al., 2012; Spaak, de Lange, & Jensen, 2014). This result contradicts the underdamped resonance model, which would predict a non-linear increase and robust maintenance of phase only during rhythmic stimulation. While two studies report the occurrence of phase-locked alpha activity suddenly occurring more than one second after the offset of the stimulus (Jensen, Bonnefond, & VanRullen, 2012; Samaha, Bauer, Cimaroli, & Postle, 2015), these results are biological implausible given the non-stationarity of alpha and the temporal precision of the visual system, as well as directly contradicted by a thorough attempts to replicate such effects (van Diepen, Cohen, Denys, & Mazaheri, 2015). Overall, the lion's share of evidence suggests that most of large-scale SSRs measured at the level of EEG and MEG during and following 10 Hz repetitive stimulation result from the superposition of evoked activity. The results are consistent with each transient evoked response containing a strongly damped alpha oscillatory response to an individual external stimulus. This pulse may or may not result from the abrupt realignment of on-going activity, though the lack of credible post-stimulus phase maintenance suggests such alignments measured at the scalp are short lived.

If alpha-band activity plays a key causal, functional role in visual perception, it is likely that the broad, regional coherence of alpha activity measured via the field potential does not adequately capture the nature of that role. The LFP response of the neural subpopulations may be completely washed

out or distorted by the regional alpha signal, representing hundreds of thousands of neurons associated with different receptive fields, or otherwise not actively involved in processing a specific external visual input. With the exception of two-photon spectroscopy, which only functions in animal models at single locations, current neuroimaging techniques lack the specificity to separate the rhythmic activity of sub-populations of neurons within a region. It is possible that sustained, relatively stationary alpha activity occurs among specific neural subpopulations, and that such activity is entrained to visual stimulation with an undetectable effect on the local field. The measurement of behavioural outcomes during and following visual entrainment may be able to circumvent these limitations of brain imaging.

Alpha Entrainment and Perceptual Modulation

An alternative approach to studying the outcome of rhythmic visual stimulation though neuroimaging is to measure it through changes in behaviour. In 2010, Mathewson and colleagues proposed that rhythmic visual stimulation within the alpha-band (12 Hz) would lead to rhythmic fluctuations in subsequent masked target detection, matching the phase dependencies previously found in relation to endogenous alpha activity (Mathewson, Fabiani, Gratton, Beck, & Lleras, 2010). They presented either one, two, four or eight annuli at a rate of 12 Hz, before the onset of a masked target with final-item to target delays between 32 and 130 ms. They found a marked decrease in the report of the target at “out-of-phase” delays (23, 130 ms SOA) compared to “in-phase” delays (83 ms SOA) when two or more items were presented. This finding was replicated in a follow up simultaneous EEG study, which also included a regular vs irregular stimulation condition (Mathewson et al., 2012). The authors found that increased phase-locking at the time of the target at 12 Hz to low vs. highly irregular streams was correlated with differences in 83 ms detection performance between low variability and high variability trials within the irregular condition.

However, only modest differences were found between the hit rates under the regular and irregular condition, with the same peak in performance at ~83 ms SOA in both conditions. Since these initial findings, a number of labs have described behavioural fluctuations which have been attributed to endogenous brain oscillations (Cravo, Rohenkohl, Wyart, & Nobre, 2013; Fiebelkorn, Saalmann, & Kastner, 2013; Hickok, Farahbod, & Saberi, 2015; Landau & Fries, 2012; Song, Meng, Chen, Zhou, & Luo, 2014). De Graaf and colleagues found small phasic benefits in two-alternative forced choice, near-threshold target identification (de Graaf et al., 2013). The frequency of the behavioural benefit for each individual correlated with the frequency of occipital resting state MEG alpha activity. Spaak and colleagues used lateralized regular vs. irregular stimulation to demonstrate behavioural fluctuations in lateralized, near threshold target detection, connecting performance to lateral asymmetries in MEG alpha activity (Spaak et al., 2014). These studies conclude that alpha-band visual entrainment is a powerful tool for the production and investigation of neural oscillatory activity.

If repeated visual stimulation at alpha frequencies leads to frequency–selective, substantial changes in visual perception, much of the work of the last thirty years using rapid-serial visual presentation (RSVP) paradigms may be re-examined in a new light. One particularly important finding in the field is the attentional blink, the inability to report the second target in a stream of targets when the delay between targets is ~200-500 ms. As Hanslmayr and colleagues point out, nearly all studies of the attentional blink involve the presentation of items at a rate of 10 Hz (Hanslmayr et al., 2011). Martin and colleagues found that the attentional blink was reduced during irregular vs. regular 10 Hz presentation, suggesting that the temporally regular condition increased alpha activity, leading to an internally oriented state (Martin, Enns, & Shapiro, 2011). Zauner and colleagues go so far as to declare that alpha entrainment is the cause of the attentional blink, as an increase in alpha power and phase locking was found for trials in which the second target went undetected (Zauner et al., 2012). Furthermore, if visually entrained alpha-band inputs result in the same behavioural outcomes as endogenously produced oscillations, visual stimulation at 10 Hz should impact a number of visual

cognitive functions, such as the encoding and maintenance of items into visual working memory (Myers, Stokes, Walther, & Nobre, 2014).

Overview of the Present Study

In the current work, we directly address the role of rhythmic visual entrainment in the alteration of visual perception. In Chapter 2, we start by attempting to find a causal role for alpha oscillations in the attentional blink, and conclude that visual entrainment at a rate of 10 Hz does not substantially, selectively alter blink magnitude. In Chapter 3, we test the hypothesis that the rapid presentation of non-target information at the alpha frequency leads to overall suppression or phasic inhibition of single target identification, and find the evidence overwhelmingly does not support this claim. In Chapter 4, we revisit and attempt to replicate previous studies that had previously reported evidence of phasic alternations in perception resulting from rhythmic entrainment. We fail to replicate the results of both experiments, and offer alternative explanations for the current results. In Chapter 5 we test the temporal acuity of the visual system to repeated vs. changing objects, and find that temporal acuity in humans is substantially hindered by object change, particularly at frequencies at or above 10 Hz. However, no relationship is found between alpha entrainment and anisochrony detection. We conclude in Chapter 6 that rhythmic visual stimulation at the alpha-band frequency range does not selectively lead to macroscopic changes in visual perception matching the putative pulsed inhibitory role of alpha activity in gating visual perception.

Chapter 2: Alpha Entrainment and the Attentional Blink

Introduction

The visual system takes time to process and store incoming visual information. Attention thus acts as a filter to select the most important, task critical information at the expense of subsequent information. Perhaps the most well-known example of this is the attentional blink (AB) phenomenon; when two visual target items are embedded as part of a rapid series of items, the second target will often be missed if it occurs 200-500 ms after the first target (Raymond, Shapiro, & Arnell, 1992). When the first target (T1) is task irrelevant, the second is generally reported, demonstrating that the loss of the second target (T2) is due to the attention devoted to the first, rather than a pure sensory deficient. Thousands of articles have been written examining the nature of the attentional blink deficient over the past 20 years (See Dux & Marois, 2009; Martens & Wyble, 2010), though the nature of the AB remains somewhat unresolved. In a recent review, Hanslmayr and colleagues put forward the proposition that the attentional blink is, in part, due to a shift from an externally oriented state to an internally oriented state of visual processing (Hanslmayr et al., 2011). An externally oriented state is necessary for the collection of new incoming information with high fidelity, whereas an internally oriented state is ideally suited for maintaining selected objects in working memory and matching to held template information. The authors propose that alpha activity forms part of the substrate of such as process. During an internal state, such as triggered following the first target, increased occipital alpha inhibits the processing of further sensory information through pulsed inhibition, while promoting cross-regional coupling of retained information. Endogenous alpha phase had already been demonstrated to partially predict the success or failure of masked single target perception (Hanslmayr et al., 2007; Mathewson et al., 2009). This framework in relation to the AB was supported by studies which report greater resting state alpha power in individuals with larger AB magnitudes (MacLean, Arnell, & Cote, 2012) as well

as greater alpha phase synchronization just before the second target when the second target is missed (Kranczioch, Debener, Maye, & Engel, 2007; Zauner et al., 2012).

Hanslmayr and colleagues further point out that the lion's share of previous work on the attentional blink has been conducted using an RSVP rate of ~8-12 Hz. As rapid alpha-band visual presentation is known to result in the phase locking of matching frequencies in the occipital lobe, it is possible that the RSVP stream entrains alpha activity to a phase which is poor for perception. This theory predicts that any disruption of such alpha "entrainment" should facilitate processing of the second target. Indeed, Martin and colleagues reported that the introduction of temporal jitter, by varying the ISI of an RSVP stream (17 to 153 ms ISI, 12 Hz average rate) before T1 and T2 substantially reduces the magnitude of the blink (Martin et al., 2011), which could be attributed the disruption of alpha entrainment. No difference in AB magnitude between regular and irregular stimulation was found in a subsequent study of the AB (Zauner et al., 2012), though the authors argued that the irregular stimulation used was insufficient to disrupt alpha entrainment (+-20 ms). Any explanation for the attentional blink must also take into account the "skeletal blink"; the presence of the attentional blink when only four items are presented (two targets and two masks) (Duncan, Ward, & Shapiro, 1994; McLaughlin, Shore, & Klein, 2001). The presence of the skeletal blink, however, could be accounted by the presence of endogenous alpha activity in the absence of rapid stimulation, leading to an endogenous "internal" state at each target onset, and the loss of T2 processing.

With this framework in mind, Elwyn Martin, Simon Hanslmayr, Jim Enns, Alejandro Lleras and Kimron Shapiro proposed that only an alpha-band (8-12 Hz) RSVP stream will lead to a substantial attentional blink (unpublished). To test this hypothesis, Martin and colleagues presented an RSVP stream of task irrelevant grey letters at theta, alpha, beta and gamma rates. Two pop-out red targets were embedded in-phase with the stream with lags of ~100, 300 or 700 ms, adjusted to maintain the rhythmicity of the stream until the occurrence of T2. After T2, the RSVP in all conditions reverted to a rate of 10 Hz. Initial tests appeared to show the presence of an attentional blink only for the alpha

(10 Hz) stimulation condition. Unfortunately, this result may have resulted from a subsequently discovered error in stimulus presentation.

Experiment 1

The design and methods used in Experiment 1 resulted as a follow-up to unpublished work previously conducted by Elwyn Martin, Simon Hanslmayr, Jim Enns, Alejandro Lleras, and Kimron Shapiro. Experiment 1 is a redesign of this work with moderate modifications. [1]

In Experiment 1a (N = 24), participants had to identify two target red letters that appeared in rapid succession embedded in an RSVP stream of distractor black letters (Figure 2.1). The two red target letters (T1 and T2) had 3 possible SOAs of ~100 ms, ~300 ms , or ~700 ms, with the middle SOA selected to match the strongest time point of the attentional blink (lowest T2 performance). Black distractor letters were presented at 4 different speeds (6.3 Hz, 10 Hz, 16 Hz, and 36 Hz) separated in a block design. Experiment 1b (N = 24) was the same as Experiment 1a, except participants were told to ignore the first red letter. Experiment 1b served as a control experiment to demonstrate the attentional nature of the blink observed in Experiment 1a, with the expectation of no blink when the first red item is not a target.

Methods

[1] The work of the current chapter regarding the attentional blink was conducted in collaboration with Elwyn Martin, Simon Hanslmayr, Jim Enns, Alejandro Lleras and Kimron Shapiro. I was asked to replicate the results of the previous experiment with a new presentation script, faster LCD monitor, and modifications on the previous design. Specifically, to address a concern that the absence of a non-alpha blink may have been related to the temporal irregularity of a frequency switch after T2 in all but the alpha condition, I changed the design such that the post-T2 period maintained the frequency of the preceding stream. All other modifications were minor. The hypothesis remained the same; only alpha-band stimulation would lead to a substantial attentional blink. The design of Experiment 2 and the final interpretation of the results are my own.

Twenty-four participants (mean age: 19.5 years, 21 female) took part in Experiment 1a. Participants were to be excluded if overall performance across all conditions fell below 50% (Chance: 33%), and by this criteria no participants were excluded from analysis.

Stimuli were presented on a 27" ASUS VG278HE LCD monitor with a grey-to-grey response time of 2 ms, set to a refresh rate of 144 Hz. Participants were seated approximately 70 cm from the display. All letter stimuli were presented in Arial Bold 36 point font (~ 1° visual angle in diameter) for three frames (21 ms) each against a grey background (RGB: [127 127 127]), all distractor letters were black (RGB: [0 0 0]) and all target letters were red (RGB:[255 0 0]). The first target (T1) was always one of three letters (B, G or S); the second target (T2) was one of a different set of three letters (X, K, or Y). Each trial consisted of the central, serial presentation of distractor letters (the remaining 22 non-target letters of the English alphabet, randomly selected with replacement) and two target letters, presented at one of four different frequencies (6.3 Hz, 10 Hz, 16 Hz, or 36 Hz, blocked). Within a trial, the time between each letter presentation was held constant, such that the letter series was completely isochronous. A trial began with 500 ms of a blank grey screen, followed by the serial presentation of distractor stimuli for ~1000 ms before the presentation of T1, and for ~550 ms after the presentation of T2. The time interval between the first and second target (lag) was manipulated to be approximately 100, 300 or 700 ms for each sequence frequency. The exact time intervals between T1 and T2 for each sequence frequency and lag can be found in Table 1, and the corresponding number of intervening items can be found in Table 2. A black asterisk immediately following the final distractor item cued the participant to report T1 and T2, and the next trial followed immediately after T2 report. A diagram of the trial timing can be found in Figure 2.1.

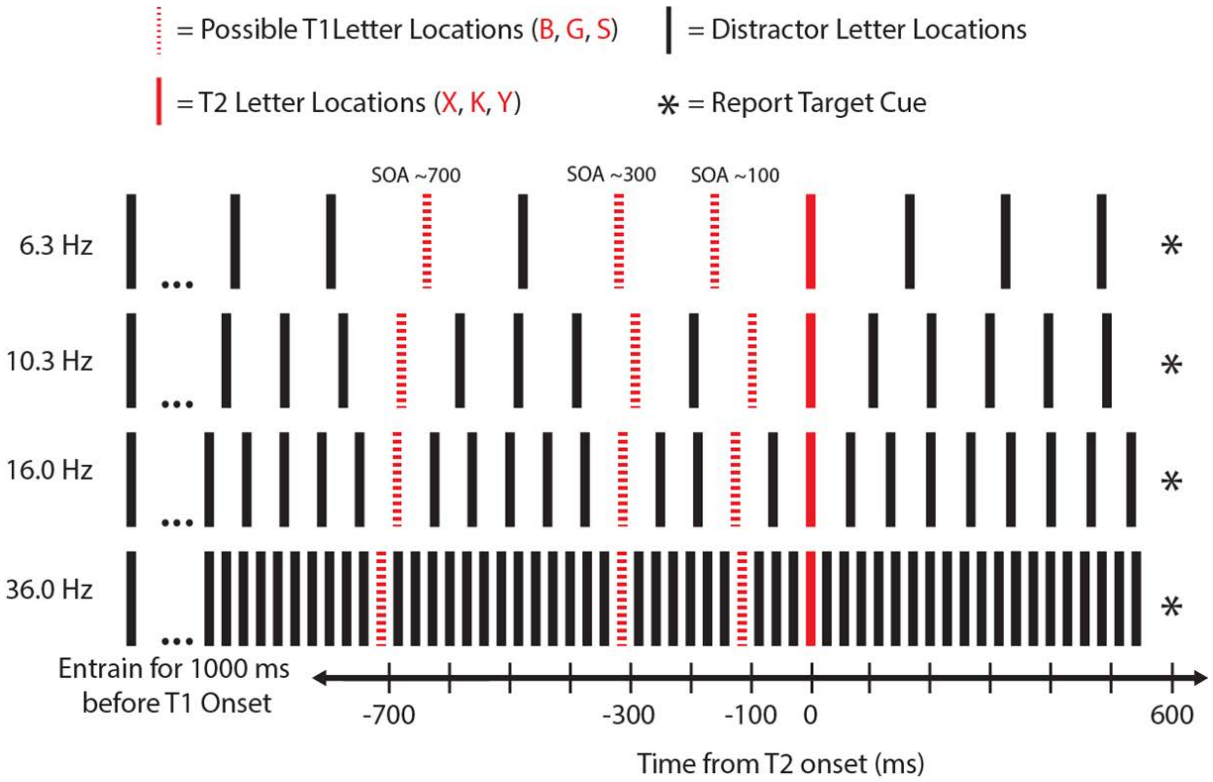

Figure 2.1 Trial design of Experiment 1. Each vertical line represents the timing of presentation of a single letter. Letters were presented at one of four different frequencies on a given block, with block order counterbalanced across participants. In Experiment 1a, T1 was to be reported, in Experiment 2, participants were instructed not to report T1.

Table 1: Exact interval parameters for each frequency (ms)

	Lag		
Frequency	100ms	300ms	700ms
36.0 Hz (Gamma)	111	306	694
16.0 Hz (Beta)	125	313	688
10.3 Hz (Alpha)	97	292	681
6.3 Hz (Theta)	160	319	639

Table 2: Number of stimuli between T1 and T2, for each frequency x lag condition.

	Lag		
Frequency	100ms	300ms	700ms

36.0 Hz (Gamma)	3	10	24
16.0 Hz (Beta)	1	4	10
10.3 Hz (Alpha)	0	2	6
6.3 Hz (Theta)	0	1	3

Participants were explicitly told and shown the possible letter identities of T1 and T2 before the experiment, and were asked to identify and report the two red letter targets in order. Only responses corresponding to one of the three possible letters for each target position were accepted, thus participants had to select from three independent, alternative choices for each target position. Thus, chance accuracy for each target was 33%, and order reversals were not possible. Participants selected each letter by pressing the corresponding button on the keyboard.

Each participant completed four blocks of 81 trials, one block for each sequence frequency, for a total of 324 trials. Each block contained a counterbalanced and randomly ordered set of 81 trials from a 3x3x3 design (T1 identity, T2 identity, Lag). Frequency block order was fully counterbalanced across participants. Participants were given a brief self-paced break between blocks.

The methods and procedures used in Experiment 1b were identical to Experiment 1a, except that the participants was instructed to only report the second red letter target, and only a single response corresponding to one of the possible T2 identities was recorded. Twenty-four participants (mean age: 19.1 years, 22 female) participated in Experiment 1b.

Analysis

To examine differences in the magnitude of the attentional blink across frequency in Experiment 1a, we conducted a repeated measures one-way ANOVA of AB magnitude, defined as the % correct difference in performance between T2 accuracy for all trials in which T1 was correctly identified (T2|T1) at Lag 700 minus Lag 300. T2|T1 accuracies at Lag 100 are included to examine the extent of

Lag 1 sparing in the current paradigm, though not included in the calculation of AB magnitude. We also conducted a repeated measures one-way ANOVA on T1 accuracy, regardless of lag, to examine the effect of frequency on target visibility. For Experiment 1b, a repeated measures one-way ANOVA of general target accuracy (second red letter) was conducted. To determine the change in AB magnitude resulting from ignoring T1, a mixed effects two-way ANOVA (Frequency x Group) was conducted comparing the magnitude of the blink between Experiment 1a and 1b. All reported statistics were Greenhouse-Geisser corrected for violations of sphericity and all pairwise statistics were Bonferroni corrected for multiple comparisons. We also performed independent one-sample t-tests on each frequency bin to determine if the AB magnitude was significantly larger than chance for each frequency condition.

Results

In Experiment 1a, we found a significant main effect of Frequency ($F(3,69) = 7.13$, $p = .002$, partial $\eta^2 = .643$) on AB magnitude (See Figures 2.2 and 2.3). Pairwise comparisons revealed a significantly larger blink for the 10.3 Hz and 16 Hz conditions than the 6.3 Hz and 36 Hz conditions (all $p < .05$), with no other significant differences between conditions. AB magnitude was significantly larger than zero at 10.3 Hz ($p = .012$) and 16 Hz ($p = .006$), while AB magnitude was not significantly different from zero at 6.3 Hz ($p = 0.56$) and 36 Hz ($p = .22$). Thus, an AB was observed at both 10 Hz and 16 Hz, contrary to the initial alpha entrainment hypothesis. T1 accuracy was significantly different between conditions ($F(3,69) = 43.2$, $p < .001$, partial $\eta^2 = .831$), with accuracy falling monotonically as a function of frequency, as would be expected due to an increase in forward and backward masking of the task-irrelevant stimuli with increasing frequency.

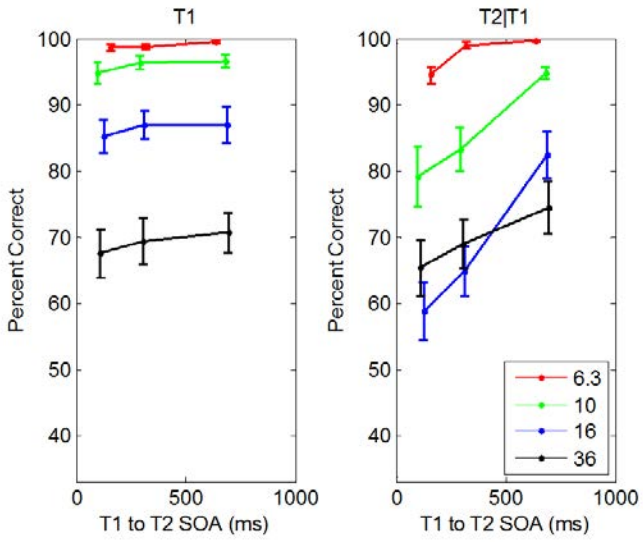

Figure 2.2 The results of Experiment 1a. Error bars represent the across participant standard error.

In Experiment 1b, when participants were instructed not to report T1, the overall magnitude of the blink was significantly reduced compared to Experiment 1a ($F(1,46)$ = 12.6, p = .001, partial η^2 = .215) (See Figure 2.3), demonstrating that the blink produced in the current experiment was due in large part to the allocation of attention and the top-down selection of T1, rather than pure bottom-up stimulus properties, consistent with previous AB literature.

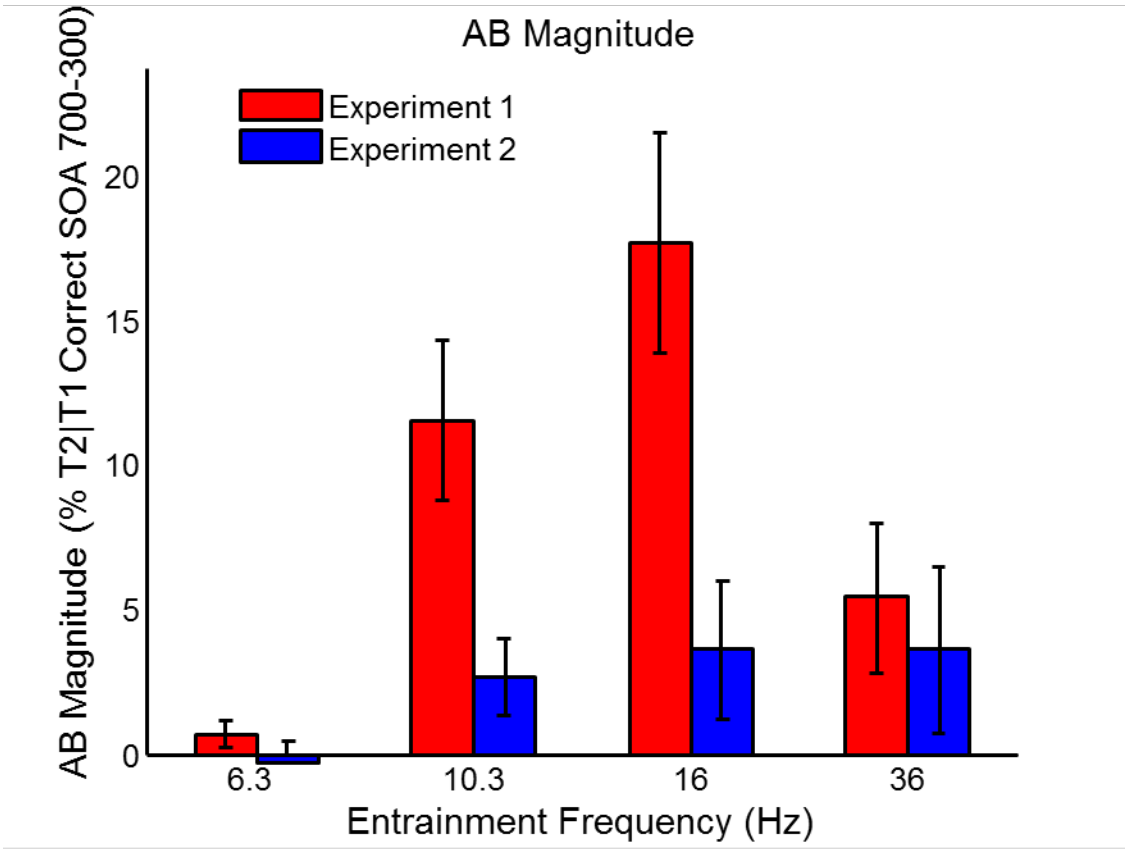

Figure 2.3 AB magnitudes from Experiment 1a and 1b and T1 accuracy from Experiment 1a. Error bars represent the across participant standard error.

Thus, the results were inconsistent with the hypothesis that only stimulation at alpha band (10 Hz) would produce an attentional blink, as an equal or greater blink was occurred when items were presented at a rate of beta band (16 Hz). However, the results of Experiment 1 do not preclude a substantial role of entrainment in producing the attentional blink. For instance, it is possible that both stimulations at 10 Hz and 16 Hz lead to inhibitory entrainment at 10 Hz and 16 Hz, respectively, or that both lead entrainment of a single critical band of activity between 10 and 16 Hz (i.e. .,high-alpha, low-beta). The synchronization of both alpha and beta-band activity are often altered by sensory events in concert (Klimesch, 2012) and both bands are reportedly correlated with T2 performance on a trial-by-trial basis (Glennon, Keane, Elliott, & Sauseng, 2015; Gross et al., 2004).

This alternative alpha/beta entrainment hypothesis could explain the absence of the blink at in the 6.3 Hz and 36 Hz conditions. However, these results could be adequately explained by the two stage model of the blink by Chun and Potter (Chun & Potter, 1995). According to this model, T2 processing is delayed by the appearance of the first target, leading to subsequent interference when T2 +1 occurs ~100 ms later. In the theta (6.3 Hz) condition, both T1 and T2 accuracy were near ceiling, which could be attributed to the lack of effective backward masking from the T1+1 and T2+1 items (160 ms SOA). It has been well established that a sufficiently delayed T2+1 will lead to the absence of the blink, irrespective of the stream frequency. Likewise, the reduced or absent blink in the gamma (36 Hz) condition could due to the backward and/or forward masking of T2 and/or T1. In addition, the reduction in T1 accuracy in the gamma condition, combined with a three-alternative forced choice task (3AFC), likely led to the inclusion of a significant number of "T1 correct" trials in which T1 was not perceived (i.e., guessed correct T1), skewing the results of T2|T1. Finally, the magnitude of the blink produced at 10 and 16 Hz using the paradigm employed in Experiment 1a was small compared to most blink paradigms, putting to question the generalizability of the results.

Experiment 2

In Experiment 2, we sought to distinguish between the Alpha/Beta Entrainment account and the Chun and Potter account of the attentional blink, while addressing the additional concerns of the blink magnitude and generalizability of Experiment 1. First, we changed the task to the report of letters embedded in a series of task irrelevant digits, a paradigm known to produce a large attentional blink. We also adjusted the timing of T2+1 to be equal in all conditions to more closely equate backward masking, removed the item immediately preceding T2 from the gamma condition to prevent excessive forward masking of T2, and adaptively adjusted the luminance of T1 to better match T1 performance between conditions. As the pre-T2 frequencies were largely maintained, as in

Experiment 1, the Alpha/Beta Entrainment account predicts a substantial blink only at 10 and 16 Hz, while the two-stage model predicts a blink for all conditions (See Figure 2.4).

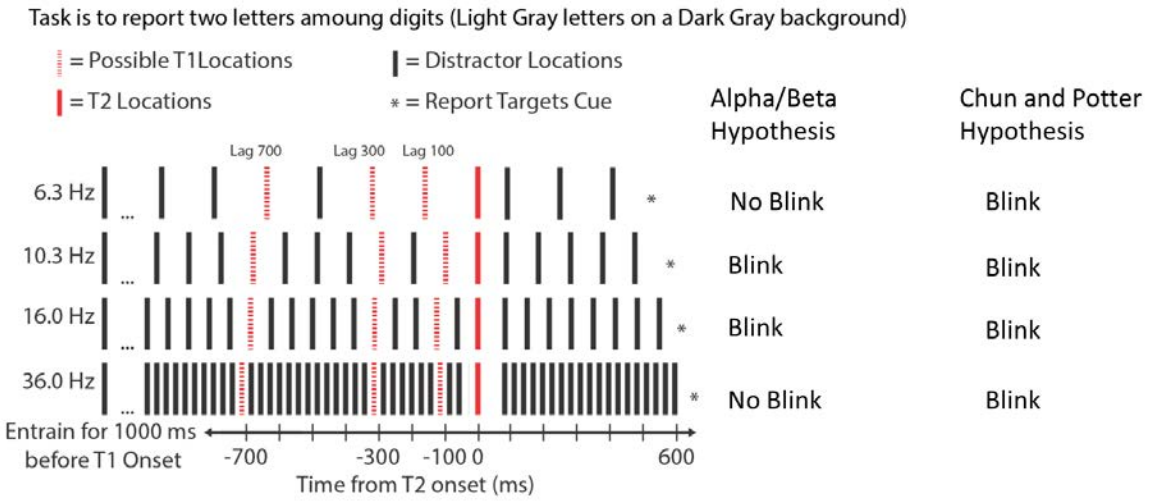

Figure 2.4 Temporal trial design and predictions of Experiment 2 according to each account.

Methods

Experiment 2 was the same as Experiment 1 except as follows:

Twelve participants (mean age: 21.8 years, 9 female) participated in Experiment 3. Frequency order was counterbalanced across participants using a random Latin square design. The task was to report two letters presented among digits, in order to increase the depth of the attentional blink compared to Experiment 1. The stimuli were changed such that all distractors were randomly selected from the digits '1' through '9', with the constraint that the same digit would never be presented twice in a row within a trial. Targets were selected from all 26 letters of the English alphabet, with the constraint that T1 and T2 would never have the same identity within a trial. Subjects were explicitly informed that 'O' should be viewed as a letter, not the number zero. Participants were told they

could report each target letter in any order, and responses matching either target were marked as correct at the position presented, regardless of the order in which the response was input. Participants were forced to make two different letter responses before the trial would continue. Pure chance T1 or T2 performance was 8%.

All digits and letters except for T1 were light grey (RGB: [128 128 128]) presented on a black background. Courier font was used instead of Arial, due to poor spatial overlap between letters and numbers in Arial font (still ~1° visual angle). In order to better equate the overall accuracy of T2, the time between the onset of T1 and the following distractor was fixed at 97 ms for all conditions, and the distractor immediately preceding T2 (T2-1) in the Gamma condition was no longer presented (i.e. the T2-1 SOA changed from 28 to 56 ms) to reduce the forward masking of T2. No other changes to the timing of the trial sequences were made (See Figure 2.4).

To approximately equate T1 performance across frequency, the luminance of T1 relative to all other items (relative contrast) was manipulated for each frequency to achieve 80% T1 accuracy at lag 700. Pilot data was used to estimate this threshold and set initial relative contrast values to 34%, 57%, 146%, and 179% for the Theta, Alpha, Beta and Gamma conditions, respectively. Starting with these initial values, T1 contrast was adjusted in a 4-up, 1-down staircase procedure in increments of 20%, based solely on Lag 700 performance, but applied uniformly to all lag conditions. The maximum T1 contrast was capped at 200%. The final threshold values across the twelve experimental participants matched well with the initial settings (*M*: [34% 56% 137% 190%], *SD*: [13% 17% 32% 17%]). This contrast manipulation was effective at maintaining equal T1 Lag 700 accuracy in all frequency conditions excepting the Gamma condition (*M*: [82% 82% 82% 61%], *SD*: [4% 4% 5% 15%]). In the Gamma condition, nine of 12 participants had contrast thresholds at or above maximum allowed, resulting in reduced, though well above chance, T1 performance (chance = 8 %).

Each participant completed 78 trials per block, for a total of 312 trials participant. All 26 were letters pseudo randomly selected to occur exactly once at the T1 and T2 positions for each Lag, within each frequency block.

Analysis

A repeated measures one-way ANOVA across Frequency was performed for overall T1 accuracy and AB magnitude, along with all pairwise comparisons as well as tests for the presence of the blink at each frequency, as in Experiment 1.

Results

Overall T1 accuracy was significantly different between conditions ($F(3,33)$ = 13.76, p = .001, partial η^2 = .556), driven by relatively reduced accuracy in the gamma condition (p < .005 for all comparisons between 36 Hz and all other frequencies). This resulted due to some participants failing to reach 80% performance, even at the maximum allowed contrast (200%) (See Figure 2.5). Nevertheless, given that chance level performance in Experiment 2 was 8%, the T1 contrast manipulation in Experiment 2 achieved the goal of dramatically reducing the number of randomly guessed T1 correct responses.

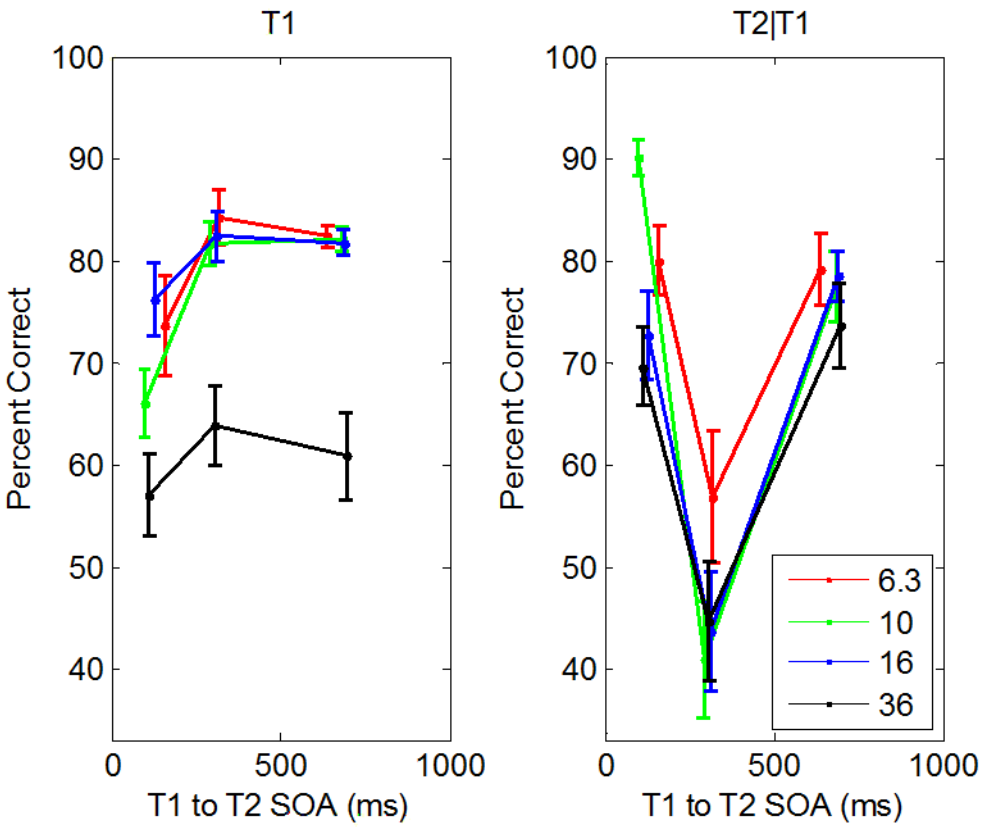

Figure 2.5 Results of Experiment 2. T1|T2 accuracy across four frequencies and three SOAs. Error bars represent the across participant standard error.

A substantial blink was observed in all conditions (p < 0.005 at all frequencies, See Figures 2.5 and 2.6). The ANOVA testing for differences in AB magnitude between frequencies was marginally significant ($F(3,33)$ = 2.59, p = .067, partial η^2 = .166), with pairwise comparisons between frequencies revealing a significantly lower AB magnitude at 6.3 Hz than 10 Hz (p = .048). No other pairwise comparisons approached significance.

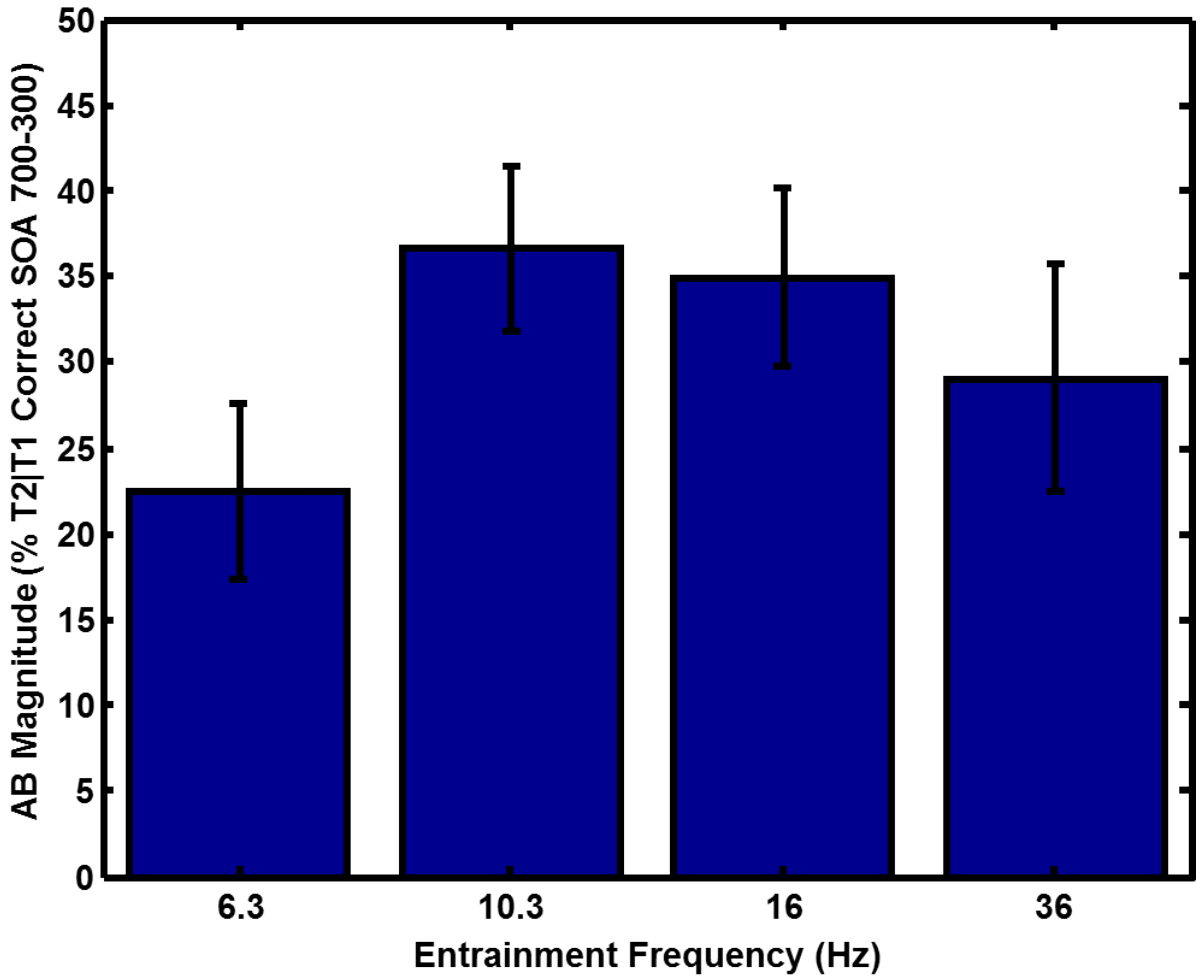

Figure 2.6 Bar plot of AB magnitude across Frequency for Experiment 2. A substantial blink is observed at all frequencies. Error bars represent the across participant standard error.

Discussion

Combined, the results of Experiments 1 and 2 are largely consistent with the two-stage model of the attentional blink, and are inconsistent with the Alpha/Beta Entrainment hypothesis of the production of the attentional blink. In Experiment 2, a substantial blink can be observed, even when stimulating at theta (6.3 Hz) and gamma (36 Hz) frequencies. The absence of a significant blink at 6.3 Hz in Experiment 1a can likely be attributed to a ceiling effect which occurs when T2 is remains unmasked for a sufficient period of time, rendering it visible even when T1 is observed. Likewise, the

modest reduction in AB magnitude in the 6.3 Hz condition in Experiment 2 is likely the result of reduced masking of T2 due to the greater spacing between T2+1 and T2+2 inherent in the design. The presence of a robust blink at 36 Hz in Experiment 2 suggests that the reduction or absence of a blink at 36 Hz in Experiment 1 could be due to either the inclusion of T2|T1 trials in which T1 was not observed and/or a near ceiling level of interference masking when T2+1 is presented at a very short SOA.

The current experiments demonstrate that the attentional blink is produced in the absence of alpha-band entrainment, and thus, such entrainment is not the causal force behind the attentional blink in RSVP paradigms. The previous assertion by Zauner and colleagues (Zauner et al., 2012) that the attentional blink is due to entrainment in the alpha-band was largely dependent on the finding of greater alpha *phase* locking at T1 and T2 for AB versus non-AB trials in the absence of a difference in alpha *power*. However, the relative maintenance of alpha phase during T2|T1 missed trials is insufficient to demonstrate a causal role of entrained alpha phase on target identification. The lowered phase locking on missed trials reported in the Zauner et al. study could be attributed to any number of cognitive processes resulting in evoked or induced EEG activity in and around the alpha band. A phase reset cannot be inferred solely by a change in phase without a change in power (Mazaheri & Jensen, 2006; Sauseng et al., 2007). The finding of Martin and colleagues (Martin et al., 2011) that the attentional blink magnitude was greater following a regular versus irregular stream could also be explained by factors other than the effects oscillatory entrainment. For instance, a temporally irregular series may capture greater attention than a temporally invariant series, regardless of stimulation frequency, leading to a reduction in blink magnitude, though the current set of experiments were not designed to directly test this hypothesis. Our results are consistent with the results of a recent study, published after the start of the current work (Janson, De Vos, Thorne, & Kranczioch, 2014), that found 12 Hz stimulation prior to T1 did not increase the magnitude of the attentional blink, 12 Hz RSVP stimulation led to a *decrease* in alpha power over the stimulation period, and that increased phase coherence following RSVP was mostly limited to the RSVP

frequency (12 Hz) rather than the endogenous frequency (10 Hz). Combining the evidence, it appears increasingly unlikely that the generation of the attentional blink is effectively manipulated by alpha-band rhythmic visual stimulation.

While the results of the current experiment appear to exclude the hypothesis that the particular frequency of an RSVP series is the driving cause of the attentional blink, the results do not preclude a modest role of entrainment on target detection. Recent studies reporting effects of entrainment on single target detection suggest changes in hit rate attributable to entrainment of between 1.5% and 15% (de Graaf et al., 2013; Mathewson et al., 2012; Spaak et al., 2014). The current experiments were not designed to test whether such subtle differences in AB magnitude could occur. Furthermore, the current experiments cannot exclude the possibility that the attentional blink is related to endogenous alpha-band activity. Although alpha-band activity is generally reduced during visual stimulation, a substantial proportion of endogenous activity continues independent of stimulation, and it's quite possible that shifts in such endogenous activity reflect shifts between external and internal processing, adjusting the likelihood of being able to report a subsequent target. However, in the absence of strong evidence directly linking alpha-band entrainment to the attentional blink, there is no reason to assume that a particular neural frequency band plays an outsized role in producing the AB phenomenon. It's been observed that the attentional blink occurs to a lesser or greater extent due to a number of semi-independent factors (Dux & Marois, 2009; Kawahara, Enns, & Di Lollo, 2006), and that changes in cross-regional brain activity across a wide range of frequencies may be independently contributing to different cognitive processes leading to the loss of T2 (Glennon et al., 2015).

The combined results of the current study highlight the need to reconsider and examine alternative explanations for changes in behaviour during and following rhythmic stimulation other than the entrainment of frequency-matched neural oscillations.

Chapter 3: Alpha Entrainment and Single Target Detection

Introduction

In Chapter 2, we provided evidence to demonstrate that the attentional blink does not substantially result from phasic visual entrainment in response to the preceding RSVP stream. However, the attentional blink is not the only cognitive phenomenon associated alpha activity. It has been proposed that rapid visual stimulation at 10 Hz leads to oscillatory entrainment and phasic fluctuations in the identification of single visual targets following stimulation (Ambinder & Lleras, 2009; Ariga, Kawahara, & Watanabe, 2011; Mathewson et al., 2010). In the seminal study by Ariga and colleagues (Ariga & Yokosawa, 2008), a sequence of 3-20 blue letters were presented at a rate of 10 Hz, ending with a white target letter followed by a final distractor letter. The authors found that the probability of correct identification of the target letter steadily increased as a function of the number of preceding task-irrelevant letters, levelling off after the presentation of approximately 10 items (~1000 ms after sequence onset). This perceptual improvement appeared to depend on the similarity of the priming sequence to the target; priming with nonsense characters was only marginally effective at improving letter detection. The authors called the phenomenon *attentional awakening*, because target detection increased "as if attention was gradually awakened from sleep" (Ariga & Yokosawa, 2008). This benefit has since been attributed to the gradual increase in entrainment of the occipital alpha rhythm with an increasing number of pre-target items, leading to enhanced perception of in-phase targets (Ambinder & Lleras, 2009; Mathewson et al., 2010, 2009).

Alternatively, the "awakening" benefit observed by Ariga and colleagues could result from a frequency non-specific benefit of rapid visual stimulation prior to the onset of the target. It has been suggested that the rapid presentation of a series at 10 Hz leads to the visual system treating the

series as a single continuous object, with each individual item processed in the context of being embedded within the object (Ariga et al., 2011). Identification of items in a series is poorer at the onset of the object, due to an initiation cost in establishing the object. It remains unknown the speed at which the series to takes on the attributes of an object, though the absence of awakening benefits following series gaps of 500 ms or greater suggests that the lower limit is likely to be above 2 Hz (Ariga et al., 2011).

We sought to test whether alpha-band rate (10.3 Hz) visual stimulation produces phasic changes in single target identification. We started by combining the approaches of Ariga et al. 2008 and Mathewson et al. 2010 to directly test this prediction.

Experiment 1

In Experiment 1, we sought to test these competing accounts by entraining participants with a RSVP stream of 6 different frequencies preceding a masked target (*Entrainment Condition*). For each frequency we included a control condition (*Foreperiod Condition*), in which only the first and last item of the pre-target sequence was presented, in order to dissociate the effect of entrainment from the costs or benefits of presenting a single non-target item at a particular SOA before the onset of the target. Finally, performance for the *Entrainment* and *Foreperiod* conditions were normalized by subtracting from each participant the target accuracy achieved when only a single pre-target item was presented one second before the target (*Single Cue* Condition). A model of visual temporal priming that is dependent on the reset of endogenous alpha rhythms would predict that the perceptual benefits of the *Entrainment* condition compared to the *Foreperiod* condition would be greatest around 10 Hz and no benefits would be observed at all other non-alpha band frequencies.

The object maintenance hypothesis would predict a benefit at a minimum frequency of rapid stimulation leads to perceptual improvements, with no particular benefit at 10 Hz.

Methods

Observers

15 participants (9 female, 6 male), aged 18 to 38, participated in Experiment 1. All participants reported normal or corrected-to-normal vision and were screened for normal colour vision with the 15 Hue Farnsworth colour test.

Stimuli and Apparatus

Both experiments were run on a PC with an Intel Core i7 chipset and Nvidia Quadro 600 dual-output graphics card. A 27" ASUS VG278HE LCD monitor with a refresh rate of 144 Hz and a grey-to-grey response time of 2ms was used for stimulus display, set to the native resolution of 1920 x 1080 pixels. Participants were seated with their eyes approximately 70 cm from the monitor. Letters were presented in size 36 Ariel font, each letter subtending approximately 1° visual angle. Letters were always presented for 3 frames (21 ms). Black (RGB: 0, 0, 0) and red (RGB: 255, 0, 0) letters were presented on a grey (RGB: 127, 127, 127) background. A single black asterisk ('*') served as the end-of-trial/response cue. 'B','G','S','X','K', and 'Y' served as red target letters, all 18 other letters in the English alphabet served as black distractors, selected randomly with replacement in every instance.

Task and Procedure

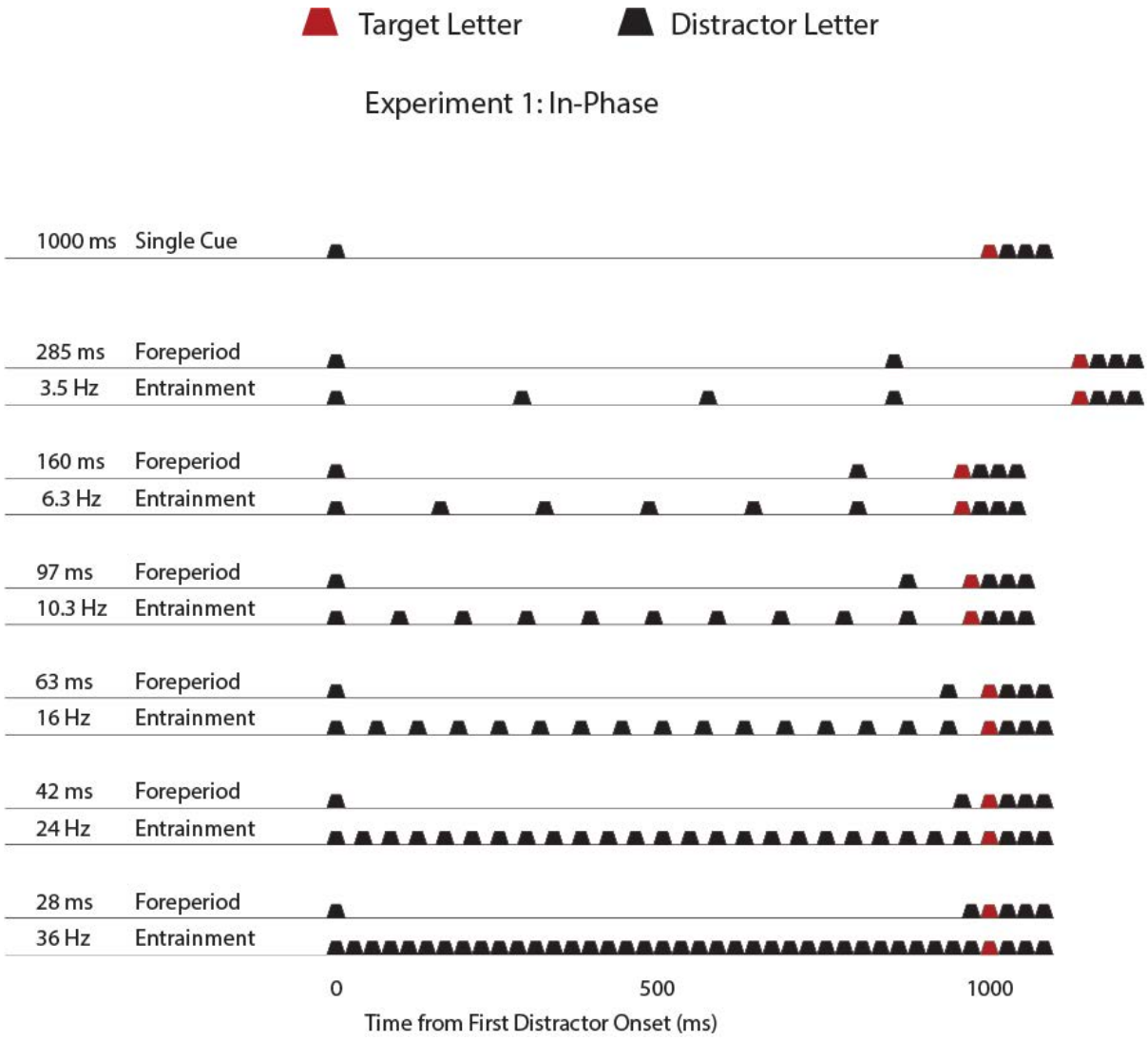

Figure 3.1. Temporal profile of each condition in Experiment 1.

Participants were asked to identify a single red letter (target) and ignore all black letters (distractors). Each trial began a completely blank grey screen, with the onset of the first distractor letter black distractor letter at the centre of the screen after 500 ms (Figure 3.1). For *Entrainment condition* trials (43%), this distractor was followed by a series of distractor letters presented at 6 different temporal frequencies (3.5 Hz, 6.3 Hz, 10.3 Hz, 16 Hz, 24 Hz, 36 Hz) selected so that the harmonics of the lower frequencies did not match the higher frequencies. The target was presented at an SOA exactly matching one cycle of the entrainment frequency (285, 160, 97, 63, 42, and 28 ms,

respectively). The time between the first distractor and the final target was held as close as possible to 1000 ms, but varied slightly depending on entrainment frequency. The red target was followed by a mask of three serially presented black distractor letters presented at 36 Hz. The end-of-trial/response cue was presented at the centre of the screen immediately following the final mask distractor, which cued the participant to select their best guess of the target letter from the keyboard. *Foreperiod condition* trials (43%) were identical to the *Entrainment condition* trials, except that all intervening stimuli between the first and last distractor before the target were removed. This served as a baseline condition that accounted for the potential attentional capture and temporal predictiveness effects of initial distractor onset and final distractor offset. Finally, during the *Single Cue condition* trials (14%), only a single distractor letter was placed exactly 1000 ms before target onset, with no intervening distractors.

16 blocks of 84 trials were presented, for a total of 1344 trials. Each block consisted with all possible combinations of six target letters, six frequencies and two conditions (*entrainment* and *foreperiod*) (72 trials), along with 2 repetitions of *single cue* condition trials for each target letter (12 trials). All trials within a block were ordered randomly. Participants were given an enforced 30-second break every 100 trials.

Results

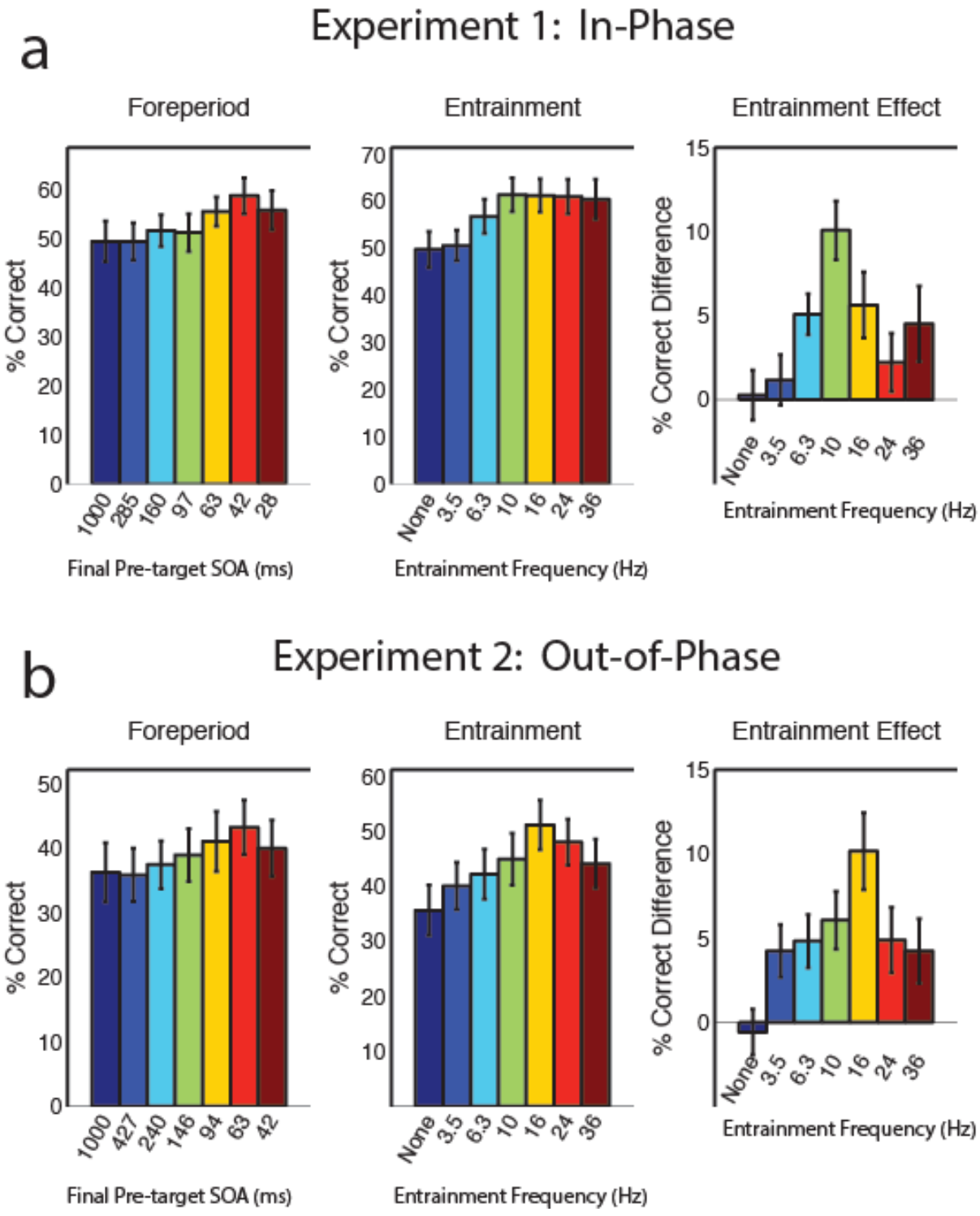

Figure 3.2. Target identification accuracy by sequence condition for a) Experiment 1 and b) Experiment 2. The Entrainment Effect represents the within participant subtraction of Foreperiod condition accuracy from Entrainment condition accuracy. Error bars represent across participant standard error.

Mean correct target identification accuracy across all conditions was 55.3% (chance = 16.7%). The key dependent variable of interest was the % correct accuracy on the target identification task in each condition after subtracting the % correct accuracy of the *Single Cue* condition for each participant, which defined the % correct benefit of the *Foreperiod* and *Entrainment* conditions (See Figure 3.2a). All results were collapsed across letter identity, leaving 6 Frequencies x 2 Types (*Foreperiod and Entrainment*) for analysis. A two-way ANOVA was then conducted (Frequency x Type). All reported statistics were Greenhouse-Geisser corrected for violations of sphericity and all pairwise statistics were Bonferroni corrected for multiple comparisons.

The two-way, repeated measures ANOVA of Frequency and Type revealed a significant interaction between Frequency and Type ($F(3.07,43.0)$ = 3.01, p = .039, partial η^2 = .177), with a main effect benefit of the *Entrainment* condition over the *Foreperiod* condition ($F(1,14)$ = 36.0, p < .001, partial η^2 = .720). Therefore, simple main effects were investigated for each of the Types. A one-way ANOVA of the *Foreperiod* condition showed significant differences in performance based on SOA ($F(2.23,31.2)$ = 5.14, p = .010, partial η^2 = .269). No pairwise comparisons between SOAs were significant. All 6 SOAs were compared pairwise to zero with a one-sample t-test, finding that the three quickest final SOAs lead to a significant target identification benefit (i.e. more accurate target identification than the *Single Cue* condition (p < 0.05, uncorrected).

An ANOVA of the *Entrainment* condition showed a significant effect of Frequency ($F(2.29,32.1)$ = 10.3, p < .001, partial η^2 = .425). Compared to the *Single Cue* control condition, target detection performance was significantly improved at all frequencies except 3.25 Hz (p < 0.05, uncorrected).

The percentage correct target identification for each SOA of the *Foreperiod condition* was subtracted from the corresponding frequency of *Entrainment condition*. We termed this difference value the *entrainment effect*, as it represents the benefit of entrainment that is not accounted for by the foreperiod cueing of the final item. Pairwise comparisons revealed that the entrainment effect at 10 Hz was significantly larger than at 3.5 Hz (p = .001). No other pairwise comparisons were significant.

The *entrainment effect* was significantly greater than zero at 6.25 Hz, 10.3 Hz and 16 Hz ($p < 0.05$, uncorrected).

Thus, the results of Experiment 1 were partially in line with both the alpha entrainment and the object-based maintenance accounts of the target detection benefits following rapid stimulation. The peak benefit of rapid pre-target stimulation appeared to occur at 10 Hz, supporting the entrainment account. However, benefits of entrainment over the matched foreperiod were also observed at non-alpha frequencies (6.3 Hz and 16 Hz), supporting the object-based maintenance account.

Experiment 2

Experiment 1 provided evidence for a benefit of visual entrainment over multiple frequencies, with a peak benefit at 10 Hz. However, it remains untested whether the benefits at any given frequency can be attributed to the phase alignment between the entraining stimuli and the target stimulus. To address this question, we conducted an experiment identical to Experiment 1, except the target time was shifted and additional half-cycle to be exactly 180° out of phase with the entraining stimulus. This manipulation allowed us to further test the predictions of the entrainment and the object-based maintenance accounts. If target detection is enhanced by "in-phase" target presentation under the entrainment account, then setting the target completely out-of-phase should result in a *decrease* in performance (i.e. a *negative entrainment effect*), particularly at the alpha-band frequency (10.3 Hz). Finally, if the benefit was due to mid-frequency object-based maintenance that is not dependent on phase, we would expect the results of Experiment 2 to be similar to Experiment 1, with positive mid-range frequency entrainment benefits.

Methods

Observers

16 participants (14 female, 2 male), aged 18 to 35, screened for normal colour vision, participated in Experiment 2.

Stimuli and Apparatus

All stimuli and equipment were identical to Experiment 1.

Task and Procedure

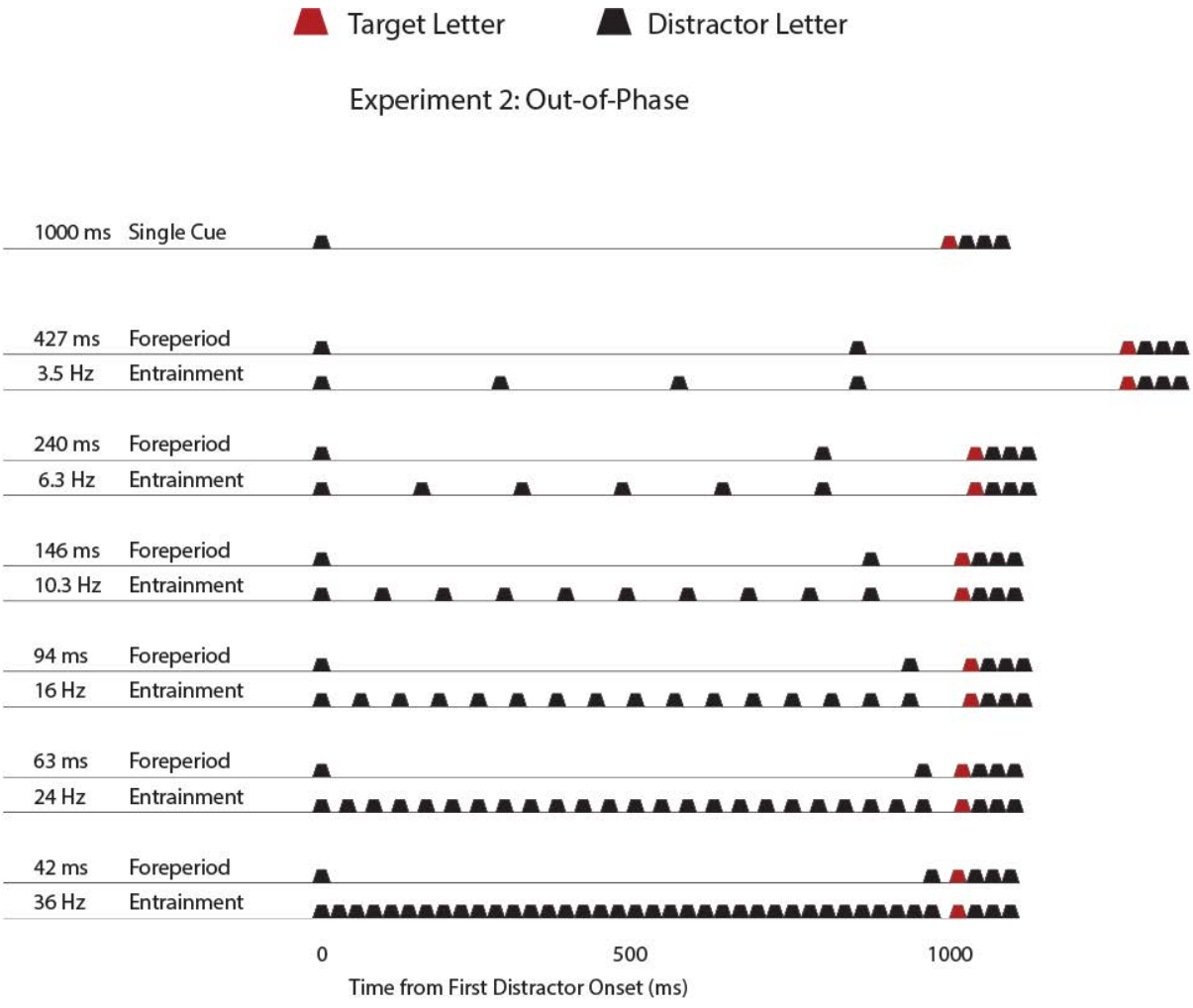

Figure 3.3. Temporal profile of each condition in Experiment 2.

The task and procedure was identical to Experiment 1, except target letters were presented one-half cycle later for each entraining frequency (3.5 Hz, 6.3 Hz, 10.3 Hz, 16 Hz, 24 Hz, 36 Hz), with the final pre-target distractor to target SOA of the *foreperiod condition* once again matched to the entrainment condition (Figure 3.3). Therefore, the new final distractor to target SOAs were 427 ms, 240, 146, 94, 63 and 42 ms. The *single cue* condition was identical to Experiment 1, with a pre-target distractor to target SOA of 1000 ms.

Results

Experiment 2

Mean correct target identification accuracy across all conditions was 41.4% (chance = 16.7%).

As in Experiment 1, the percentage correct target identification for each SOA of the *Foreperiod condition* was subtracted from the corresponding frequency of *Entrainment condition* to find the *entrainment effect* (See Figure 3.2b). A repeated measures one-way ANOVA of the *entrainment effect* across Frequency revealed no significant effect of entrainment frequency on the magnitude of entrainment benefit ($F(3.34,50.0) = 1.57$, $p < .179$, partial $\eta^2 = .095$), with all frequencies showing an entrainment benefit ($p < 0.05$, uncorrected), and a trend towards a greater benefit at 16 Hz.

Experiment 1 and Experiment 2 Comparison

We then compared the results between Experiment 1 (In-Phase) and Experiment 2 (Out-of-phase). Overall accuracy was greater for the in-phase vs. out-of-phase group ($p < .05$). Surprisingly, accuracy for the *single cue* condition was significantly greater in the in-phase than out-of-phase group ($p < 0.05$), even though these trials were identical between groups, suggesting that either the context of

out-of-phase trials led to reduced target detection performance or there was an unanticipated shift in the ability of participant population between experimental groups.

A two-way repeated measures ANOVA (Frequency x Phase Group) on the *entrainment effect* was performed, which found a main effect of Frequency ($p < .05$), but no significant main effect of Phase Group, nor any significant interaction between Frequency and Phase Group. Bonferroni corrected pairwise comparisons of frequency collapsed across Phase Group revealed that the *entrainment effect* at 10 Hz was significantly larger than at 3.5 Hz ($p < .01$) No other pairwise comparisons were significant. When collapsed across Phase Group, the *entrainment effect* at all frequencies was greater than zero ($p < 0.05$). Although not statistically significant, there was a trend such that the 10 Hz *entrainment effect* was larger in the in-phase group ($p = 0.13$) and the 16 Hz *entrainment effect* was larger in the out-of-phase group ($p = 0.16$).

Experiment 3

The results of Experiments 1 and 2 demonstrated the benefits of visual entrainment over a range of frequencies. The combined evidence from Experiments 1 and 2 is not entirely consistent with any of the previously proposed explanations for the entrainment benefit. Instead, more than one overlapping mechanism is likely required to account for the result.

The data is inconsistent with a strong version of the entrainment account. The fact that "entrainment" benefits remain, even when targets are presented out-of-phase, casts doubt on models which assume benefits are derived from oscillatory phasic entrainment. The results are also inconsistent with similar models which suggest that target identification will be enhanced due to the implicit temporal expectation of when the target will occur, driven by the preceding sequence (Jones, Moynihan, MacKenzie, & Puente, 2002). Such a model would predict a decrement or no benefit in

performance when attention is allocated to the wrong temporal position, as is the case in Experiment 2 (Out-of-Phase experiment).

The results suggest that the inter-stimulus interval (ISI) between a streaming irrelevant object and a target may have as much or more explanatory power than the specific frequency or phase of the stream itself. When an irrelevant object is presented for an extended period of time, perception of a target may be enhanced during object presentation and shortly after object offset, with enhancement peaking approximately ~80 ms after object offset. This interpretation is consistent with the previous literature (Ariga et al., 2011; Mathewson et al., 2010).

However, this benefit, previously explained by temporal tuning resulting from the entrainment of endogenous alpha rhythms, could also be explained by short-term cortical activation produced by the entraining or "priming" sequence, gradually "warming-up" the visual system to promote enhanced visual perception. It has long been known that visual stimulation leads to increased visual cortical excitation over the span of at least 1-2 seconds (Lansing, Schwartz, & Lindsley, 1959; Romei et al., 2008). Furthermore, this excitation of early visual cortex is sensitive to the frequency of stimulation, with increasing activation in areas V1-V3 with increasing frequency up to 10-18 Hz (Gauthier, Eger, Hesselmann, Giraud, & Kleinschmidt, 2012; McKeeff, Remus, & Tong, 2007). This "warming-up" of the visual system through frequency dependent, stimulus evoked increases in cortical activation could lead to improved target identification, mimicking perceptual benefits found when cortical activation is induced with modest amounts of electrical or magnetic stimulation (Fertonani, Pirulli, & Miniussi, 2011; Schwarzkopf, Silvanto, & Rees, 2011).

Fortunately, entrainment and cortical activation accounts make very different behavioural predictions depending on the temporal features of the priming sequence and the time of target onset. The entrainment hypothesis predicts that the priming sequence will produce a rhythmic suppression and enhancement of target perception dependent on target delay, with peak performance when targets are presented at a matching interval ("in-phase") with the end of the

priming sequence. Furthermore, rhythmic sequences are predicted to produce greater "in-phase" performance than arrhythmic sequences, due to the enhanced phase-locking at the entraining frequency. The rhythmic effects may be restricted to stimulation at the endogenous occipital 10 Hz rhythm (Alpha-Specific Entrainment) or may occur at any rhythm that matches the frequency of stimulation (Frequency-Matched Entrainment). In contrast, the Cortical Activation account predicts increases in target identification with increasing priming sequence frequency up to the frequency of peak activation in visual cortex (10-18 Hz) at all target delays, with equal benefit from rhythmic and arrhythmic stimulation.

In Experiment 3, we sought to test which of these accounts best explains changes in single target detection after visual stimulation. To this end, we created mathematical models for each account and compared model predictions of how the frequency of the priming sequence (priming frequency, PF) and the delay between the priming sequence and the target (target delay, TD) would lead to changes in target identification. The alpha entrainment model predicts an interaction between the frequency of the entraining stimulus and the timing of a subsequent target, such that the target is best perceived in-phase with priming sequence. On the other hand, the cortical activation model predicts no such interaction between frequency and phase, but rather predicts performance increases as the presentation speed approaches the maximal temporal sensitivity of early visual cortex (10-18 Hz).

Methods

Observers

All participants reported normal or corrected-to-normal vision and were screened for normal colour vision with the Farnsworth-Munsell dichotomous D-15 test. Participants were volunteers offered University course credit for participation. Eighty-two participants (76 female, 6 male), aged 18 to 30

years old (mean age: 19.1 years), participated in Experiment 2. Two participants were excluded for a failure to follow instructions to maintain fixation, with a planned 80 participants included in the final analysis.

Stimuli and Apparatus

A PC with an Intel Core i7 chipset and Nvidia Quadro 600 dual-output graphics card was used for stimulus presentation and data collection. A 27" ASUS VG278HE LCD monitor with a refresh rate of 144 Hz and a grey-to-grey response time of 2ms was set to a resolution of 1920 x 1080 pixels. Participants viewed stimuli from a distance of 70 cm. Letters were presented in size 36 Ariel font, each letter subtending 1° visual angle. Priming and target letters were always presented for three frames (21 ms) at the centre of the screen. Masking letters were presented for 1 frame (7 ms). All priming and masking stimuli were presented in dark grey (Lab: 35, 0,0) on a light grey background (Lab: 50, 0, 0). Priming and masking luminance contrasts were matched and selected to make the priming sequence items clearly visible while producing optimal backward masking. Target letters were presented in red, isoluminant with the background in order to differentiate the target from the priming and masking items. A single black asterisk ('*', visual angle = .5°) served as the end-of-trial/response cue. 'B','G','S','X','K', and 'Y' served as red target letters, all 18 other letters in the English alphabet served as both priming and masking stimuli, selected at randomly with replacement in all instances.

Task and Procedure

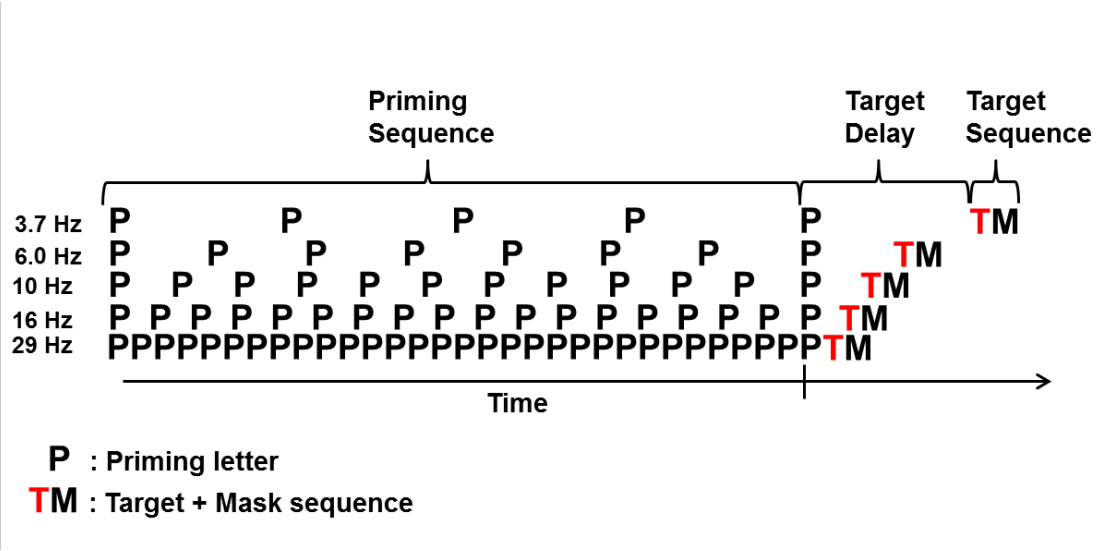

Figure 3.4. Trial structure for Experiment 3.

Participants were asked to identify a single red target letter in a six alternative forced choice (6AFC) task and ignore all dark grey letters (See Figure 3.4). Each trial consisted of the priming sequence (all items presented prior to the target), the target delay (the stimulus onset asynchrony between the final priming item and the target item), and the target sequence (the target and all subsequent masking items). Items in the priming sequence were presented at one of five possible priming frequencies (PF) on any given trial (3.7 Hz, 6.0 Hz, 10.3 Hz, 16.0 Hz, or 28.8 Hz) for a priming duration which varied uniformly across trials (1000 to 1300 ms). Thus, the number of items presented during the priming sequence varied as a function of the priming frequency and the priming duration. The priming frequencies were chosen from a natural logarithmic scale with a centre frequency of 10.3 Hz, to minimize the harmonic interference among frequencies (Penttonen & Buzaki, 2003). The priming sequence was followed by the target sequence after a delay (TD) of one of five possible durations (34.7 ms, 62.5 ms, 97.2 ms, 167 ms, or 271 ms). The target sequence always consisted of the presentation of the target, followed after an SOA of 28 ms by 9 randomly selected post-target mask letters with no inter-stimulus interval other than a 7 ms blank gap after the 3rd and 6th letter. An asterisk immediately followed the final masking letter prompted the participant to respond, and

remained on the screen until a response was made. The screen went blank for 500 ms, and then the next trial began.

As practice, participants performed 30 trials of the 6-AFC letter identification task with target letters presented at the maximal allowed red saturation within the isoluminant, grey-centred gamut of the monitor [L:50 a:70 b:70], without the priming sequence or masking stimuli. Next, the participants performed an initial staircase task (120 trials) with the masking sequence but no priming sequence, in order to estimate the participant's masked identification threshold before the main task. During this task, the redness of the target colour was adjusted in a 1-up/1-down adaptive procedure, increasing colour contrast after incorrect responses (+4 L*a*b colour units) and decreasing colour contrast after hits (-4 L*a*b colour units), starting with maximal colour saturation, thereby reducing colour saturation until an asymptote at 50% colour identification performance. Chance performance was 17%. Colour contrast of the target, rather than luminance contrast, was manipulated to ensure that target detection performance would increase monotonically with increasing colour contrast, regardless of the luminance contrast of the priming and masking stimuli. The average colour saturation value over the last 36 trials of the staircase task was then used as the starting value for target saturation in the main task.

Priming frequency, target delay and target letter identity were counterbalanced such that all 150 possible combinations (5 PF x 5 TD x 6 letters) were presented in random order for each of 5 blocks, for a total of 750 trials per participant for the main experiment, resulting in 30 trials per critical condition per participant.

To maintain equal overall difficulty and performance among participants throughout the experiment, target colour saturation was adjusted after every trial, independently, for each of the 25 PF and TD pairings, using the same staircase algorithm as the initial staircase task. Differences in performance among conditions were measured as changes in colour saturation needed to produce 50% performance. This value was normalized by subtracting the mean contrast for each condition

from the mean value over all conditions, dividing by the mean across all conditions and multiplying by 100, resulting in the % threshold benefit measure. The first 150 trials were excluded from analysis to allow contrast values to approach behavioural asymptote before calculating thresholds.

Modelling

Three models were created to explain differences in performance for all 25 combinations of priming frequency and target delay: Alpha Specific Entrainment Model, Frequency-Matched Entrainment Model and the Cortical Activation Model. The Alpha Specific Entrainment Model predicts a sinusoidal change in perception matching only the 10.3 Hz (alpha) PF trials and assumes no change in perception at other frequencies (Mathewson et al., 2010). The Frequency-Matched Entrainment Model predicts a sinusoidal change in perception matching each PF, with the phase parameter constrained to be the same value across all frequencies (i.e. all frequencies assumed to have the same "preferred" phase). Both entrainment models include a decay parameter to account for the effects of phase dispersion over time. The Cortical Activation Model predicts a change in performance by PF on a log-linear scale centred at the peak activation frequency of early visual cortex (~15 Hz) (McKeeff et al., 2007), with a parameter to account for the decay of activation. The formulas each of these models, and the criteria for initial parameter selection and the ranges of each parameter, can be found in Appendix A. The set of behavioural predictions produced by each of these models at initial parameter settings are shown in Figure 3.5.

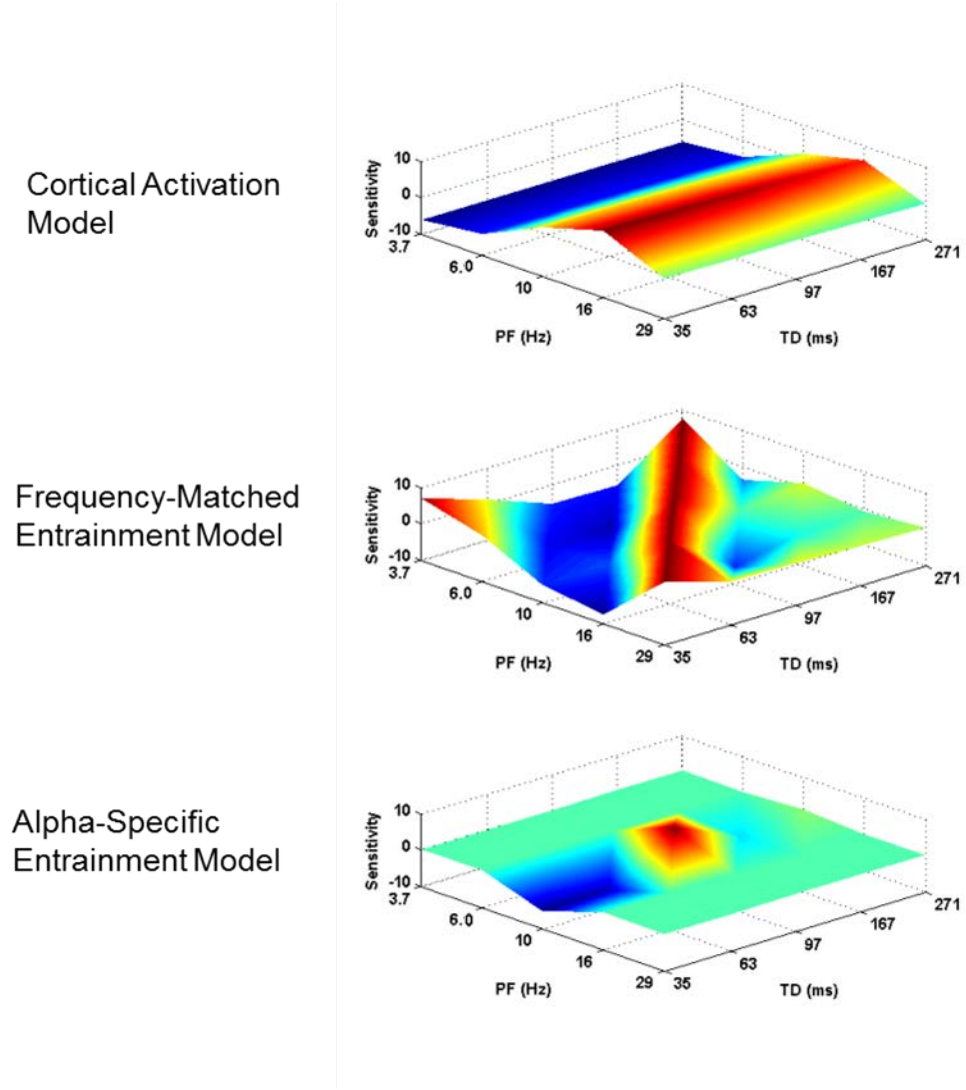

Figure 3.5. Stimulation model predictions based on initial parameters

Each model was fit to the average performance of half of the subjects selected at random, and those parameters were then cross-validated on the other half of subjects. The log-likelihood of each model was then calculated based on the measured variance between subjects, from which the likelihood of the null hypothesis (no difference between the 25 conditions) was subtracted. This procedure was repeated 100 times to acquire a bootstrapped distribution of log-likelihoods for each function. For model comparison, the Akaike information criterion (AIC) was used to adjust the log-likelihood of each model based on the number of free parameters.

Results

Priming frequency and target delay affect target identification independently

A two-factor ANOVA (PF x TD) revealed a main effect of Priming Frequency ($F(4,316)$ = 23.029, p < .001) and Target Delay ($F(4,316)$ = 6.439, p < .001) on threshold benefit.

As seen in Figure 3.6A, target identification decreased when the Priming Frequency fell below 10.3 Hz. Bonferroni corrected pairwise comparisons confirm this result (3.69 Hz < 6.1 Hz < [10, 16, 29 Hz]), with p < .005 for all significant comparisons and no significant differences between the three shorter intervals. Performance at Target Delays of 63, 97, and 271 ms was better than delays of 167 and 35 ms (Bonferroni-corrected p < .05, with the exception of p = .15 for the difference between 35 and 271 ms). No differences between 167 and 35ms, or between 63, 97, and 271 ms, were found.

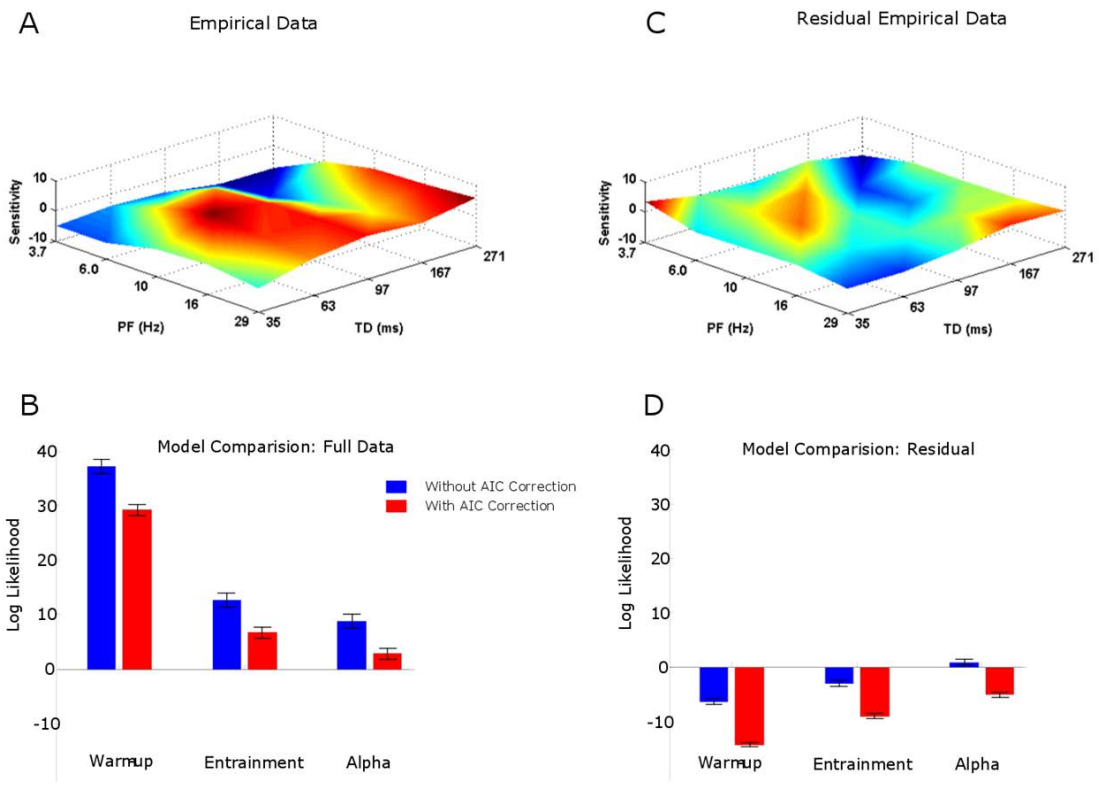

Figure 3.6. Results of Experiment 3.

The interaction between PF and TD did not quite reach significance ($F(16,1264)$ = 1.653, p = .067) as the linear, non-interactive combination of the PF and TD main effects explained the vast majority of the variance in the threshold benefit values of the 25 conditions (Pearson r^2 = .86). The lack of a robust interaction between PF and TD does not fit the hypothesis of fluctuations in identification by the Alpha Specific Entrainment Model or the Frequency-Matched Entrainment Model but rather is more consistent with the predictions of the Cortical Activation Model.

We conducted a further quantitative comparison of the three models and how well they fit the effect of stimulation on performance (see Methods). As can be seen in Figure 3.6B, the Cortical Activation Model produced a much better cross-validated fit than the best-fit produced by the other two models. This advantage remained, even after correcting for model complexity using the Akaike information criterion (AIC). This result is inconsistent with models which predict a strong oscillatory fluctuation in identification matching the "entrainment" frequency. However, even if linear-summation of frequency and delay accounted for the lion's share of the behavioural variance, it is possible that a weak oscillatory signal could account for a significant portion of the remaining variance. We therefore reran cross-validated model fitting procedure on the residual variance, subtracting the main effects of frequency and delay (linear summation) (Figure 3.6C). None of the models fit this residual better than the null distribution (Figure 3.6D). Thus, no substantial oscillatory entrainment signal could be detected, even after removing all non-interactive variance from the data.

Experiment 4

In Experiment 3, rapid, central, rhythmic visual presentation of randomly changing target-similar but task-irrelevant items lead to increasing target identification performance with increasing presentation frequency, up to 10 Hz, across all target delays. This result is consistent with the hypothesis that target-similar items prepare the visual system for perception through "warming-up" and inconsistent with oscillatory entrainment of identification performance over time. However, it remained unclear whether the presence of this rapid presentation benefit and absence of an oscillatory benefit would generalize to other types of visual stimulation. In Experiment 4, to further assess the viability of the Alpha Entrainment model compared to the Cortical Activation model, we presented the pre-target items in three Temporal Conditions: 10 Hz rhythmic (Rhythmic), 10 Hz jittered (Arrhythmic), and a control condition (Gap). In this experiment, all target items were presented at a fixed final delay of 97ms, "in-phase" with the preceding stimulation. The Alpha entrainment hypothesis predicts better target identification performance for rhythmic vs. arrhythmic stimulation. The Cortical Activation Model predicts that both rhythmic and arrhythmic stimulation will equally improve performance compared to the gap condition. In addition, we sought to test whether the benefits of the priming sequence could be driven entirely by low-level processing of any visual object, or are dependent on a categorical match between the priming and target sequence. To address this question, for each Temporal Condition (Rhythmic, Arrhythmic), we manipulated the content of the priming stream, presenting either Letters or Noise patterns as the priming sequence. If priming benefits are partially dependent on categorical target matching activation, we would expect to see a greater benefit following the presentation of Letters than Noise patterns. Finally, we sought to address the concern that any absence of rhythmic benefits could be due to the nature of the priming sequence. Previous studies demonstrating evidence for rhythmic entrainment on target detection used priming sequence items which surrounded or enveloped the target location and were identically repeated throughout the pre-target stream (de Graaf et al., 2013; Mathewson et al., 2010; Spaak et al., 2014). Thus, to test whether such manipulations would reveal evidence of rhythmic entrainment, we manipulated the format of the priming sequence for

three separate groups of participants, with the priming sequence presented centrally (Exp. 4a, *Central*), at surrounding locations (Exp. 4b, *Surround*), and with a repeated, rather than changing item, at the central location (Exp.4c, *Repeated*).

Methods

Observers

Forty-eight participants (34 female, 14 male), aged 18 to 29 years old (mean age: 22.1 years), participated in Experiment 4, with sixteen participants in each group. The same recruitment and screening procedures as Experiment 1 were used.

Stimuli and Procedures

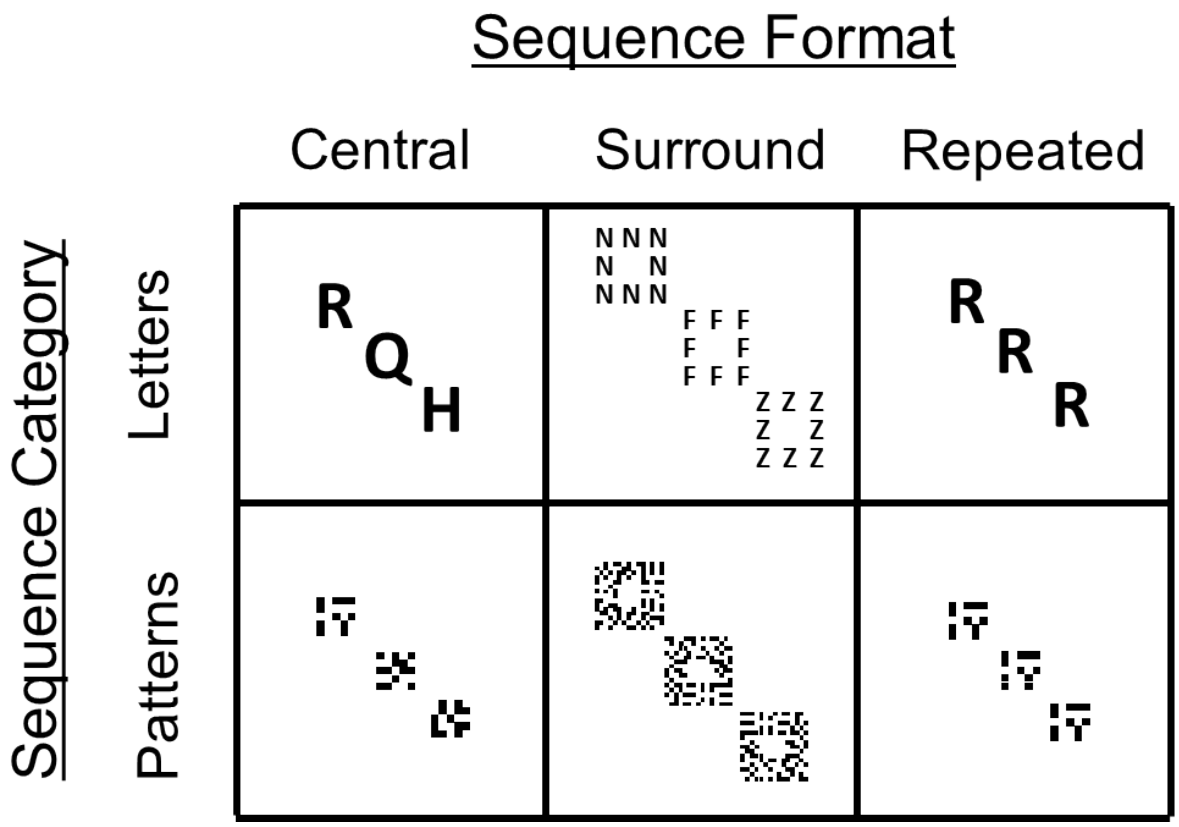

Figure 3.7 Exemplars of the first three items used in the pre-target Rhythmic priming sequences of Experiment 4a,b,c. Central, Surround and Repeated Sequence Format conditions run in three separate participant groups. Trials of each Sequence Category and Temporal Condition (See Methods) were presented randomly in a within-participant, counterbalanced mixed trial design.

All stimuli and procedures were identical to those in Experiment 1, with the following exceptions: Priming sequence stimuli for the *Central Pattern* condition were formed by randomly filling a 5x5 square central grid array (covering 1° visual angle)(See Figure 3.7). Each of the 25 squares (0.2° visual angle each) within the central grid had a 40% probability of being filled-in dark grey, and otherwise matched the background. Each Pattern stimulus was generated randomly within and across trials. The stimuli were made to approximately match the *Central Letter* stimuli in thickness, total space filled and variance in item size. The *Surround Pattern* was generated by producing a 15x15 square grid, with the 5x5 central location set to the grey background colour. *Surround Letter* stimuli consisted of a 3x3 grid of letters centred at central fixation with the central letter removed, leaving eight letters surrounding a central empty space. For the *Repeated Group*, the same non-target letter

or noise pattern was repeated throughout the priming sequence of each trial, rather than changing with each presentation. A new letter or pattern was randomly selected between each trial. Priming Sequence Category (*Letter* or *Pattern*) and Temporal Condition (*Rhythmic*, *Arrhythmic*, *Gap*) and Format (*Central, Surround, Repeated*) were manipulated in a 2x3x3 factor mixed design, with each Category and Temporal Condition tested within-subject and each Format tested between-subject (16 participants each). For the *Letter* condition, all priming sequence items were letters and for the *Pattern* condition, all priming sequence items were patterns. For *Rhythmic* trials, priming sequence items were presented for between 1000 and 1300 ms (uniform distribution), with a fixed item-to-item SOA of 97ms. For *Arrhythmic* trials, the SOA between priming sequence items varied randomly between 49ms and 146ms (uniform distribution). For *Gap* trials, all priming sequence items excepting the first and last item were removed, maintaining the same temporal distribution between first and last priming sequence item (1000 to 1300 ms).

To maintain equal overall levels of difficulty and performance among participants and between stimulus categories, target colour contrast was adjusted after every trial, independently for each of the two stimulus categories (*Letter* and *Pattern*). Target stimuli were initially set to the maximal allowed red saturation in the isoluminant, grey centred gamut of the monitor [L:50 a:70 b:70], with the a and b colour channels adjusted in the same adaptive staircase procedure as Experiment 3 resulting in a reduction in colour saturation until asymptote at 50% performance across the three Temporal conditions. Chance performance for the 6AFC task was 17%. Thus, for this experiment, differences in performance between Priming Sequence Category conditions are reflected in the 50% performance colour saturation threshold for each Priming Sequence Category condition, whereas differences between temporal conditions are reflected in accuracy (% correct) between Temporal Conditions. The accuracy of each subject in the *Gap* control condition was subtracted from the accuracy in the *Rhythmic* and *Arrhythmic* conditions to produce a measure of the benefit of stimulation for the Rhythmic and Arrhythmic conditions.

Five blocks of 144 trials were presented, for a total of 720 trials. Each block consisted with all possible combinations of six target letters, two Priming Sequence Category conditions (Letter, Pattern) and three Temporal conditions (Rhythmic, Arrhythmic, Gap). All trials within a block were ordered randomly. Participants were given an enforced break (minimum 30 seconds) at the end of every block.

Results

The results were clear and consistent (Figure 3.8). A stimulation benefit was found for all groups, with greater benefit from letter stimulation than pattern stimulation, consistent with the Cortical Activation Model. No difference was found between rhythmic and arrhythmic stimulation under any of the conditions. A 2x2x3 (*Letter*/*Pattern*, *Rhythmic*/*Arrhythmic*, *Central*/*Surround*/*Repeated*) mixed effects ANOVA with stimulation benefit as the dependent measure found a main effect of pre-target type (*Letter* > *Pattern*, $F(1,45) = 12.747$, $p < .001$) , and no other significant or near significant main effects or interactions. The lower 95% confidence bound of the stimulation benefit was above zero in all conditions. Surprisingly, stimulation appears to bestow equal benefits when stimulating surrounding locations as at the target location itself, as no overall differences in benefit were found between the *Central* and *Surround* Conditions. Benefit was also evident in the *Repeated* Condition, suggesting that stimulation variety is not necessary for preparing perception.

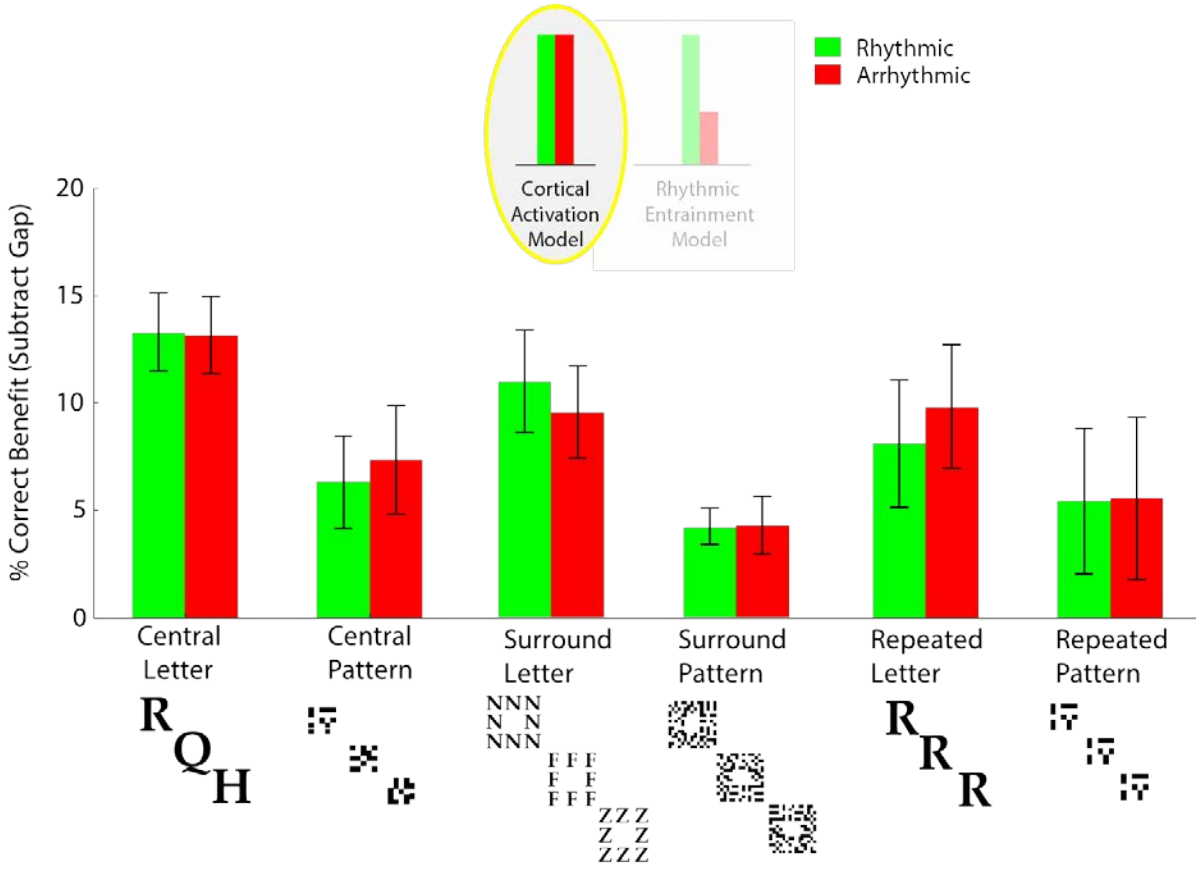

Figure 3.8. Results of Experiment 4.

Discussion

Identification of a backward masked target letter was improved when it was preceded by a stream of irrelevant items. This improvement increased with the frequency of stimulation up to 10 Hz, and was dependent on the content, but not spatial arrangement, of the priming sequence items. This benefit was not adequately explained by rhythmic entrainment, whereas the data were consistent with the notion of an activation of the visual system, briefly enhancing target perception. This study is the first to our knowledge to demonstrate that task-irrelevant, uninformative visual input preceding a target can improve perception in a sustained, non-rhythmic fashion and the first to

report the absence of the rhythmic entrainment of single target perception in response to visual stimulation at 10 Hz.

The current results are consistent with our model of a visual stimulation benefit resulting from cortical activation of relevant visual areas. The priming sequence inputs could be considered as weak, activating noise (McDonnell & Ward, 2011; Schwarzkopf et al., 2011), sufficient to activate letter processing networks, but insufficiently strong or relevant to draw resources away from the target. This account also explains the greater improvement when priming with letters than patterns in Experiment 4, as random patterns could induce overlapping activation with the target letter in early visual areas such as V1 and V2, but fail to activate ventral grapheme regions, resulting in a reduced benefit in letter identification. The equal benefit found when items were presented at surrounding locations confirms that this stimulation benefit in not of retinal origin or specific to retinotopic cortical areas.

While the results are consistent with the proposed model of cortical activation, there remain alternative accounts which could contribute to this frequency and category dependent "warming-up". For instance, an object-file initiation based account (Ariga et al., 2011; Holcombe, Kanwisher, & Treisman, 2001; Hommel, 2004; Kahneman, Treisman, & Gibbs, 1992) proposes that the maintenance of the stream as an continuous object, without a gap, enhances the perception of embedded features (target letter). It is possible that when items are presented at faster frequencies, the priming sequence is perceived as a single object, whereas at slower frequencies, each priming letter is processed as another event, capturing resources and hindering subsequent target identification. Another potential contribution to the stimulation benefit is release-from-masking, as exposure to the items in the priming sequence could reduce the efficacy of the masking items (Drew & Shapiro, 2006). Further study will be needed to disambiguate the contribution of each of these accounts.

In contrast to the substantial overall benefit of continuous visual stimulation, no evidence was found to support the hypothesis that visual entrainment would affect target identification in a rhythmic fashion. Despite a large sample size and significant main effects of both frequency and final delay, no interaction between these two factors could be found, as expected in any extant model of rhythmic entrainment. This result was confirmed through quantitative model comparison. In Experiment 4, across six different pre-target conditions, temporal jitter of the pre-target items failed to produce any changes in identification of the target letter, as would be expected under the entrainment model. The visual stimulation benefits found in the current study are inconsistent with a rhythmic entrainment based account.

The absence of the rhythmic entrainment of identification performance in the current study cannot rule out the possibility of its existence under other conditions. All previous studies finding evidence of entrainment altering single target perception involved near-threshold detection or binary identification of simple shapes or Gabor patches (de Graaf et al., 2013; Mathewson et al., 2012, 2010; Spaak et al., 2014). The current task involved the identification of a supra-threshold target letter, which participants often reported to have detected ("saw red"), even when the identity of the letter could not be accurately reported. Visual identification is a slower process than detection, requiring recurrent activity that may be less susceptible to rhythmic entrainment once target detection has been successfully established (Neri & Heeger, 2002). The current study also differed in the manipulation of the colour contrast, rather than the luminance, of the target stimulus. As colour was chosen as a target defining feature, the current paradigm may not have detected rhythmic changes restricted to the magnocellular system. If rhythmic entrainment does occur under certain conditions of target detection or identification, future studies of rhythmic entrainment would benefit from the current approach of formal modelling and comparison to alternative hypotheses, such that the nature and boundary limits of rhythmic entrainment effects can be firmly established.

In conclusion, a perceptual benefit occurs after rapid visual stimulation with task-irrelevant stimuli. This benefit does not rely on a rhythmic tuning of perception as predicted by the entrainment hypothesis, but is rather a sustained enhancement of target identification. If increased cortical activation in relevant neural networks is responsible for this enhancement, “warming-up” is likely to occur in modalities other than vision, and may reflect an inherent property that can be used to optimize performance on a variety of tasks and goals.

Chapter 4: A Failure to Replicate Entrainment of Single Target Detection

Introduction

In Chapter 3, we failed to find evidence to support the hypothesis that frequency specific stimulation at 10 Hz results in phasic entrainment of target identification. This result is somewhat in contradiction to previous studies which have attributed non-linear changes in target perception to the pre-target rhythmic entrainment of endogenous alpha-band oscillations. However, there are a number of differences between the paradigm used in Chapter 3 and previous studies of entrainment that could account for this discrepancy. To investigate the conditions under which the behavioural phasic entrainment of perception may occur, we sought to re-examine and replicate the results of previous studies reporting rhythmic fluctuations in perception following alpha-band visual stimulation. To our knowledge, there are four extant studies reporting frequency-matched, rhythmic changes in perception following alpha-band (8-12Hz) visual stimulation in humans (de Graaf et al., 2013; Mathewson et al., 2012, 2010; Spaak et al., 2014). We chose to attempt to replicate and extend two behavioural paradigms in order to address efficacy and boundary conditions of visual entrainment (Mathewson et al., 2011; Spaak et al., 2014).

Experiment 1

In the seminal work discussed in the Introduction (Mathewson et al., 2010), Mathewson, Fabiani, Gratton, Beck, and Lleras presented a varying number of metacontrast masking rings at 10Hz,

leading to a relative increase in detection when the target was presented at an 83 ms delay ("in-phase") relative to "out-of-phase" delays. All target were followed by a final metacontrast mask at a fixed post-target SOA of 45 ms. This benefit was quite substantial, with entrainment potentially account for a ~20% upward shift for in-phase target identification after eight item entrainment relative to a control condition. However, in a subsequent study, Mathewson and colleagues used a similar paradigm, but instead of varying the number of items, they varied the temporal regularity of the "entraining" series while measure ongoing activity with EEG (Mathewson et al., 2012). The magnitude of this phasic behavioural fluctuation was positively related to increased alpha power. Mathewson and colleagues decided to further split the irregular trials on the basis of the degree of temporal variability, comparing high vs low variability trials. Trials with high temporal variability appeared to produce a less phasic behavioural response than rhythmic trials, while low variability trials and rhythm trials were virtually identical. The authors concluded that alpha entrainment of perception is most effective during conditions of high alpha power and is insensitive to small irregularities. However, the results did not unequivocally support the entrainment hypothesis. Both the rhythmic and irregular conditions led to a peak in target identification at a target delay of 83 ms, in contrast to alpha phase locking measured at the scalp, which was strong during the regular series and effectively absent during the irregular series. Thus, we considered that much of the phasic benefits attributed to entrainment in the 2010 and 2012 experiments could be due to factors other than the resonance or gradual phase alignment of alpha activity.

We sought to determine the distinguishing characteristics of this behavioural non-linear response by replicating the paradigm of Mathewson 2012 with modest modifications. To determine whether the "entrained" oscillation is sustained at the entraining frequency (12 Hz) over several cycles, we extended the maximum target delay from 177 ms to 341 ms. We also increased the ratio of catch (no target) trials to 50%, allowing for the testing of response bias at each individual target delay, which was not possible in the 2010 and 2012 designs due to the infrequency of catch trials (20%) used. We found that performance on this near-threshold detection task without feedback was highly

variable, with ceiling performance for most and floor performance for some. In Mathewson et al. 2012, the issue was a floor effect, which led to the exclusion of four out of seventeen participants (23%) on the basis of less than 9% performance on the Rhythmic condition, an undesired *a priori* expectation and a somewhat biased and seemingly arbitrary procedure for determining subject inclusion. Therefore, we sought to roughly equate overall performance between participants by adjusting the luminance of the target in a threshold determination task prior to the start of the main task.

Methods

The current experiment was designed to replicate the methods, stimuli and procedures used by Mathewson et al. 2012, with some deviations from the previous design to specifically examine effects of rhythmic vs arrhythmic entrainment over a broader time window, limit the number of participants excluded due to poor performance, and adequately account for response bias (false positives). The methods were as follows:

Fourteen participants (Age: 19-38 years, *M*= 26.6 years, 9 female, 5 male) participated in the experiment for payment. One participant did not complete the main task, due to poor performance on the thresholding task (performance below 75% at the maximum target contrast).

A PC with a 17 Hz CRT monitor and a refresh rate of 85 Hz was used for stimulus presentation, calibrated to a standard gamma value of 2.2. Participants were seated 60 cm from the centre of the screen with their chin placed in a chinrest.

Participants viewed all stimuli against a fixed grey background (RGB: [128 128 128], 9.6 cd/m^2). Each trial began with the presentation of a black fixation cross (0.3° visual angle) for 258 ms, followed by a black interval of 412 ms, followed by the priming sequence. The priming sequence consisted of the

serial presentation of eight annuli (outer radius: 1.0°, inner radius: 0 .5°, RGB: [64 64 64], 2.0 cd/m^2) at central fixation (See Figure 4.1). For the Rhythmic Condition, the eight annuli were presented serially at central fixation for two frames (23 ms) each, with a fixed stimulus onset asynchrony of SOA of 82 ms (12.1 Hz), over the span of 588 ms. For the Arrhythmic Condition, the timing of each annulus between the first and eighth annulus was varied randomly, with the constraint of a minimum SOA of three frames (35 ms) between annuli and a fixed SOA between the first and eighth annulus (576 ms) to match the Rhythmic Condition.

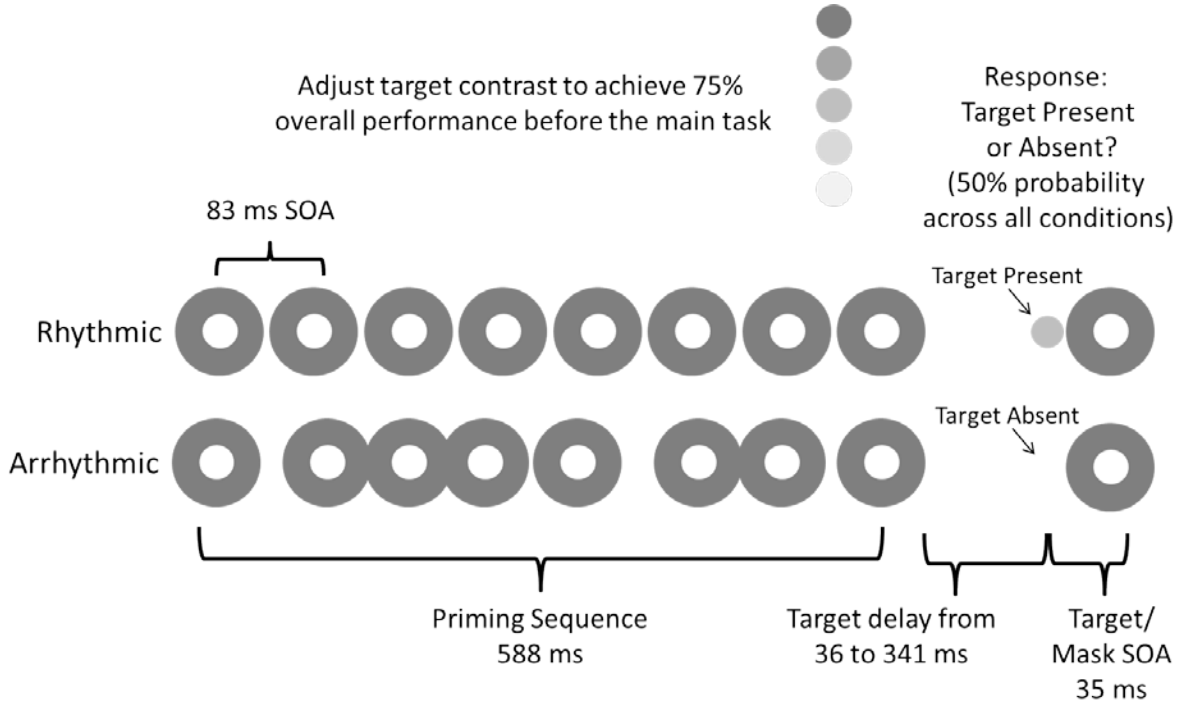

Figure 4.1 Task/sequence design for Experiment 1.

The priming sequence was followed after a delay by the target/mask sequence. On Target Present trials, the target/mask sequence consisted of the presentation of a filled grey circle (radius: 0.5°) for one frame (12 ms) followed by a two frame (23 ms) blank interval, followed by a final annulus (23 ms), which served as the metacontrast mask of the target. On Target Absent trials, the target was replaced with a blank interval. After the target/mask sequence, a 306 ms blank interval was presented, followed by the fixation cross, which cued the participant to respond. The fixation cross remained on the screen until a response was given and then the next trial would begin.

The target delay was defined as the delay between the onset of the final annulus of the priming sequence and the target. The range of this delay was between three and twenty-seven frames (36 to 341 ms) at two frame (23 ms) intervals, for a total of 14 possible target delays.

The task of each participant was to report the presence or absence of the target during the response period of each trial, by pressing '1' or '2' on a keyboard to indicate target presence or absence, respectively. Participants were given no feedback. The main task consisted of 15 blocks, with 112 trials performed in each block, for a total of 1680 trials. Rhythmicity of the priming sequence (Rhythmic, Arrhythmic), target delay, and target presence were counterbalanced within each block in a 2x14x2 design, such that each stimulus combination appeared exactly twice in each block, for a total of 60 trials per condition of interest (30 target present, 30 target absent).

Before the main task, participants completed two blocks of 112 trials with a staircase procedure to determine the 75% accuracy threshold across all experimental conditions (the thresholding task). For the thresholding task, the target was initially set 25% darker than the background (25% contrast), and the target luminance was adjusted after each correct trial (0.5% contrast decrease) and incorrect trial (1.5% contrast increase), regardless of the experimental condition. The mean target luminance of the last 56 trials of the thresholding task was fixed as the target luminance for all conditions during main task (*M*= 56.3% contrast, *SD*= 26.1%). The thresholding procedure was effective in achieving the desired overall 75% correct performance for each participant on the main task (actual *M*= 73.5%, SD=10.3%).

Analysis

Under the entrainment hypothesis as proposed by Mathewson and colleagues, the frequency of the sustained entrained oscillation will match the 12 Hz frequency of presentation, leading to a matching sinusoidal fluctuation in target detection rates, and the reduction or absence such fluctuations

following arrhythmic presentation. In particular, the difference between rhythmic and arrhythmic stimulation should be well described by a sinusoidal function. This fluctuation could be modelled with the following equation with three free parameters:

$$f(PF, TD, \alpha, \beta, \theta) = \alpha\cos\left(2\pi PF \times \left(\frac{1}{TD}\right) + \theta\right) + \beta$$

where $PF$and $TD$are independent variables and (α, β, θ) are free parameters. PF is the frequency of annuli presentation (12 Hz), TD is the target delay, α is amplitude of the change in response rate, θ is the phase of the response sinusoid and β is the base response rate.

Alternatively, if changes in response result from forward masking response, the response rate could be modelled from a logarithmic function, as in the following equation with three free parameters:

$$f(TD, \alpha, \beta, \gamma) = \alpha e^{\beta TD} + \gamma$$

where TD is an independent variable and $(\alpha, \beta, \gamma)$are free parameters. In this case, α is amplitude of the change in response rate, β represents the steepness of the change in response rate over time, and γ is the upper asymptote of the response rate.

Results

As can be seen in Figure 4.2 both Rhythmic and Arrhythmic stimulation led to a primarily monotonic increase in target detection accuracy, with increasing hit rate with increasing delay. The change in hit rate can be closely fit with a logarithmic function (Rhythmic: R^2 = 0.966, Arrhythmic: R^2 = 0.936), with a rapid increase in target detection from 35 to 82 ms, gradually reaching asymptote, consistent with the effects of forward masking on target detection. Subtracting the hit rate in the Arrhythmic condition from the Rhythmic condition for each participant, we found no evidence of a 12 Hz sinusoidal difference in hit rate over time between the two conditions (R^2 = 0.004). A repeated

measures one-way ANOVA confirmed a main effect of Delay ($F = 3.747$, $p < .001$), along with a marginal main effect of Rhythmicity ($F = 3.747$, $p = .054$), with an overall higher target detection rate for the Rhythmic than Arrhythmic condition. No interaction between Delay and Rhythmicity was found ($F = 0.002$, $p = .968$). Thus, no evidence was found to support the hypothesis that rhythmic stimulation would lead to rhythmic fluctuations in target detection matching the priming frequency.

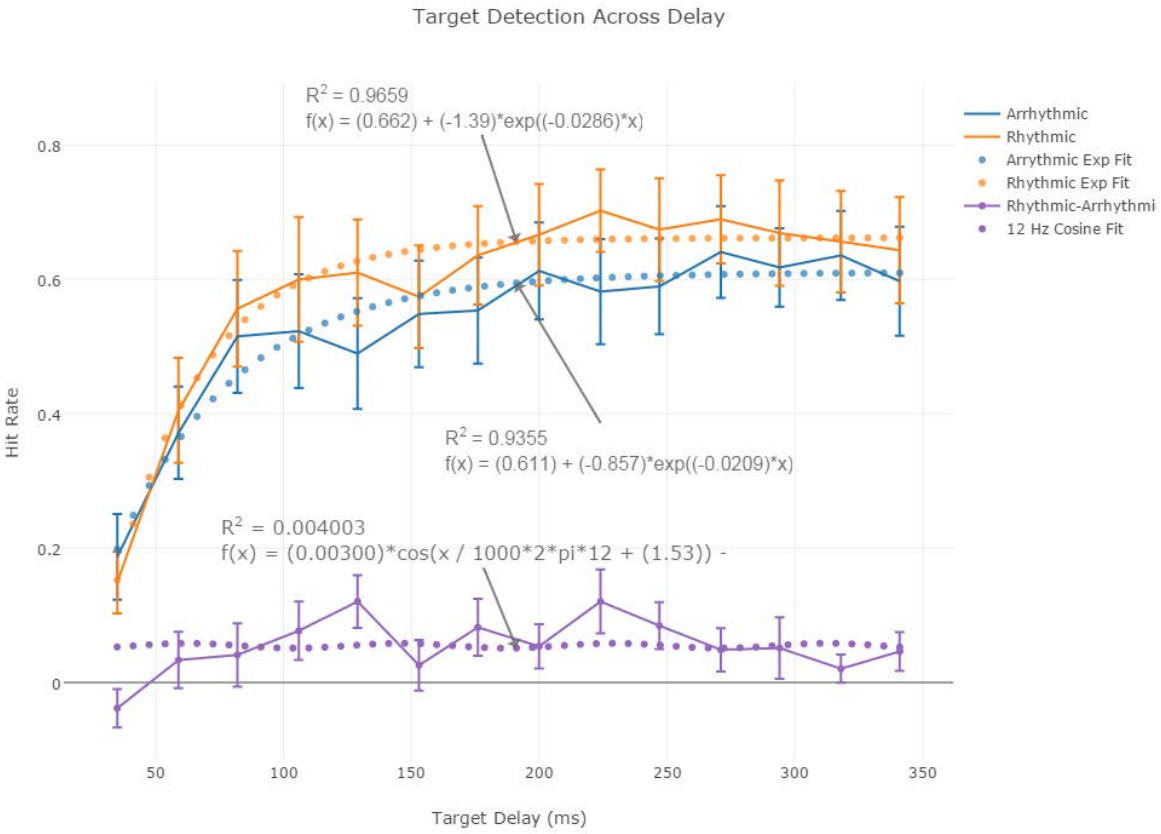

Figure 4.2 Hite rate by Target Delay. Error bars represent across participant standard error from the mean. All curves are fit to minimize the variance by adjusting all three free parameters.

To examine whether the marginally significant change in hit rate between the Rhythmic and Arrhythmic conditions could be accounted for by a response bias toward reporting a change, we compared the false alarm rates between conditions (See Figure 4.3). The false alarm rate showed a main effect of Rhythmicity ($F = 4.277$, $p = .0394$), with a greater number of false alarms in the Rhythmic condition. No effect of Delay ($F = 1.499$, $p = .222$) or interaction between Delay and Rhythmicity ($F = .279$, $p = .598$) were found, consistent with an overall shift in criterion towards a 'Target Present' response following Rhythmic vs Arrhythmic stimulation.

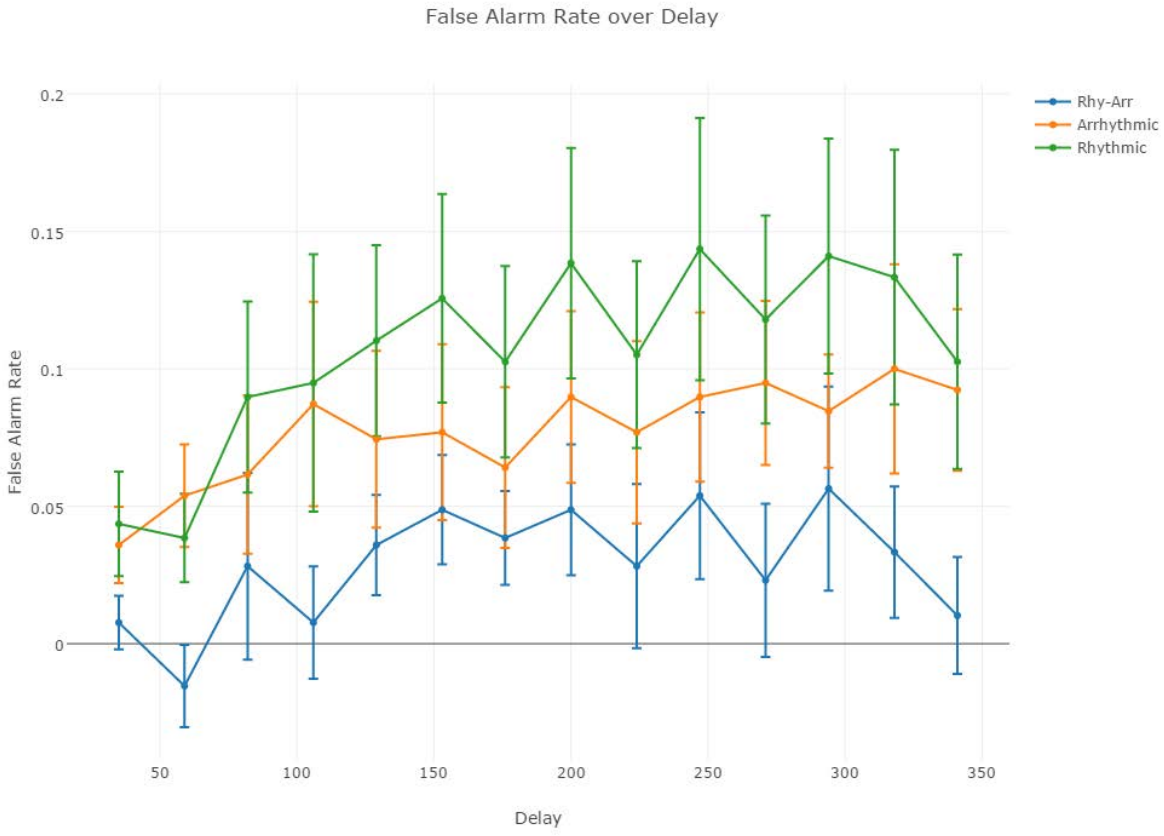

Figure 4.3 FA Rate by Target Delay. Error bars represent across participant standard error from the mean.

Overall, the results of Experiment 1 provided no evidence to support the rhythmic entrainment hypothesis. Rather, the results replicate the well-established phenomenon of forward masking of a low contrast target, which decreases as delay increases. The greater hit and false alarm rate for the Rhythmic compared to the Arrhythmic condition across most delays suggests participants exhibited a bias towards reporting a target 'Present' following Rhythmic stimulation compared to Arrhythmic stimulation, whether the target was present or absent. This bias did not oscillate at a rate of 12 Hz, as expected by the frequency-matched entrainment model. Rather, this difference between the Rhythmic and Arrhythmic conditions may have been caused by a previously unconsidered aspect of the design: the timing of the backward mask. The backward masking annulus was presented out-of-sync with the preceding annuli for 13 out of 14 delays, regardless of the absence or presence of the target, and this temporal irregularity following rhythmic stimulation may have occasionally been confused for near-threshold target detection.

Overall, the behavioural results are somewhat inconsistent with the results of Mathewson et al. 2012. While both the current study and the former study reported an increase in target detection with increasing target delay from 35 to 83 ms, Mathewson et al. 2012, reported a substantial drop in target detection from 106 to 154 ms that was not observed in the current data. It is unclear what manipulation or difference in experimental conditions could have caused this discrepancy. As the previous pattern of performance was produced twice by the same author, it is unlikely to be the result of a statistical fluke, but rather could be due to a variation in the design or experimental procedures. The known changes to the procedure in the current design are the inclusion of a wider range of delays, the exclusion of the two-item control condition, and the contrast thresholding procedure used to equate performance across participants. Any of these changes, or an unknown variable in the experimental setup or participant pool, could have contributed to the change in outcome. Nevertheless, the current experiment stands on its own as a demonstration of a condition under which rapid, rhythmic visual stimulation does not lead to observable rhythmic fluctuations in masked target detection.

Experiment 2

Finding an absence of evidence to support the rhythmic entrainment of target detection using the meta-contrast mask paradigm, we sought to replicate the results of another paradigm previously used to test the visual entrainment hypothesis of target detection. In 2014, Spaak and colleagues tested for the effects of repeated 10 Hz visual stimulation while simultaneously recording MEG activity. In this paradigm, white squares were flickered in the left and right lower visual field against a grey background for 1.5 seconds, followed by a near-threshold sine-wave grating target presented at either the left or right stimulation location at delays from 17 to 333 ms. [2] On each trial, the square on one side would flicker at exactly 10 Hz ("Entrained"), while the square on the opposite side would be presented 16 times at an inconsistent rate ("Non-Entrained"). The participant's task was to report on which side the target was presented. The authors found that regardless of flicker condition, target detection accuracy increased as function of time with a linear increase across delay accounting for more than 80% of the variance in each condition. However, the hit rate difference between targets presented in the location of the Entrained and Non-Entrained square appeared to contain an oscillatory pattern at a rate of 10 Hz. The authors then compared performance at "in-phase" (100 ms, 200 ms) vs. "antiphase" (150 ms, 250 ms) target delays and reported that a significant difference in hit rate between in-phase and anti-phase only occurs at the Entrained location. The authors further report a significant increase following stimulation in both occipital alpha power and phase-locking (ITC) in the hemisphere contralateral to the Entrained location compared to the ipsilateral hemisphere, which the authors interpret as evidence for location specific neural entrainment at 10 Hz. The authors further report that increased alpha power over sensors contralateral to the Entrained stimulus led to a larger difference in performance between the in-

[2] The maximum delay is listed as 340 ms in the original Spaak 2014 article. We have confirmed from the original author that this was a minor rounding error (i.e., 17 m x 20 delays rather than 16.666 x 20 delays).

phase and antiphase delays, leading them to the conclusion that alpha entrainment was a causal factor in determining subsequent performance. Overall, Spaak and colleagues presented perhaps the most compelling evidence and arguments to date for the existence of visual alpha entrainment of brain and behaviour.

However, there is an issue with the analysis approaches selected by the authors which may have led to spurious conclusions, as the analysis procedure used to compare ”in phase” and “antiphase” performance was biased due to the increase in delay with increasing performance. Specifically, the “in-phase” delays of 100 ms and 200 ms would be expected to have poorer performance than the “antiphase” delays of 150 ms and 250 ms, as the “antiphase” delays are affected less by forward masking, which accounted for most of the variance. Accounting for this bias, there is no longer any distinction between the magnitude of the 10 Hz fluctuation in behaviour between the Entrained and Non-Entrained conditions. To demonstrate this, we manually transposed the hit rate data provided in Figure 1B of Spaak et al. 2014, and fit a logarithmic function to the hit rate across delay for the Entrained and Non-Entrained conditions individually to account for the effect of forward masking. The residual of each of these fits was taken to represent the change in performance not accounted for by a monotonic function. Fitting a 10 Hz sine wave to the residual of each condition, we find that the evidence of a sinusoidal fluctuation in performance is nearly identical for both the Entrained and Non-Entrained conditions (See Figure 4.4). Thus, no evidence remains that the behavioural fluctuation was local to the rhythmically stimulated hemifield. An entrainment-based explanation for this account would require attributing the sinusoidal pattern in hit rate in the Non-Entrained hemifield to either an inverted influence of rhythmicity on perception at the contralateral location or a delay dependent response bias that is independent of target presence. As the Entrainment Index (EI) used by the authors is based the difference between “in phase” and “antiphase” time points, it is significantly biased by monotonic changes in behaviour over time. It can also be expected to be highly volatile due to chance, given the number of trials collected, as each the four inputs to the index are calculated on the basis of 9 trials each (20% of the data collected). The correspondence

between the EI and contralateral alpha activity could alternatively be attributed to a shift in the slope of forward masking or a fluke of chance. Finally, the phase of the 10 Hz oscillatory pattern in behaviour observed (antiphase to the Entrained stimulation rather than in-phase) was not the predicted pattern *a prori*, requiring an additional free parameter and increasing the probability of a spurious result. Still, while the explanation for each individual analysis is open to alternative interpretation, the authors make a compelling case for visual entrainment as the most parsimonious interpretation of the pattern of alpha activity along with the presence of the 10 Hz behavioural fluctuation.

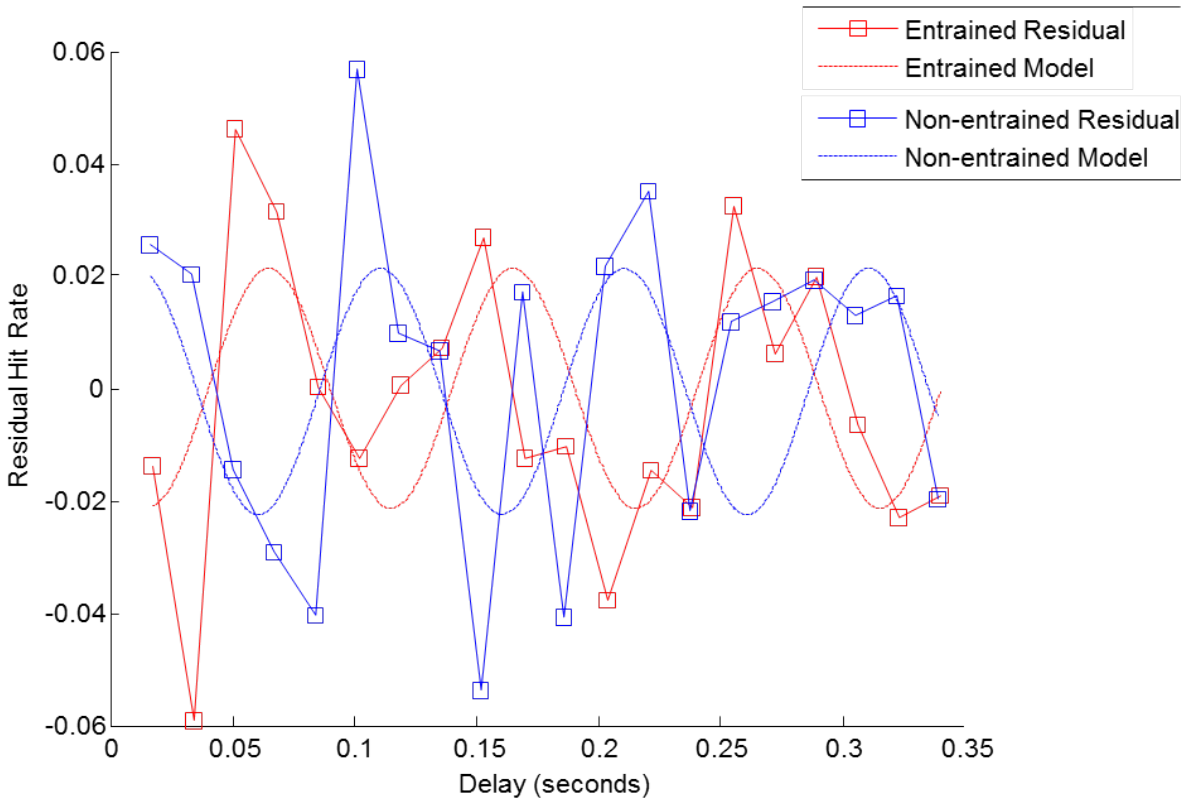

Figure 4.4 Residual in Hit Rate across Delay after removing a logarithmic fit on the Entrained and Non-Entrained Conditions (Spaak 2014 Data). The raw residual values for each condition are represented in filled lines. Ten Hz sinusoidal models were fit to each residual, presented as dotted lines for each condition. Model amplitude and phase were fit as free parameters for each residual. As can be seen, the amplitude of the 10 Hz sinusoidal pattern found in the residual of the Non-Entrained condition is nearly identical to the Entrained condition, but with inverse polarity.

The behavioural paradigm used by Spaak and colleagues is an excellent candidate for replication. The task is simple and straight-forward, and the bilateral two alternative forced choice design makes it less reliant on shifts in criterion than the present-absent judgement used by Mathewson et al. 2012. Unlike Mathewson et al. 2012, Spaak and colleagues provide a concrete model of the difference between the Entrained and Non-Entrained conditions, estimating a sinusoidal fluctuation in behaviour with an amplitude of ~4%, ~230° out-of-phase. With the phase parameter predicted *a priori*, one fewer free parameter is needed and the power to test the reproducibility of the previous result increases. Thus, in Experiment 2, we sought to replicate the behavioural work of Spaak and colleagues, with minor modifications. If the behavioural results of Spaak 2014 could be replicated, particularly the 10 Hz fluctuation in hit rate between the Entrained and Non-Entrained conditions, an important piece of evidence in support of the entrainment hypothesis would be confirmed, and we could begin to explore the boundary conditions, such as hemispheric specificity, in which visual entrainment is likely to occur. If an entrainment consistent result is disconfirmed, the visual entrainment hypothesis may no longer be the most parsimonious explanation for changes in perception following rapid stimulation.

Methods

Sixteen participants (Age: 19-38 years, *M*= 25.1 years), 11 female, 5 male) participated in the experiment.

The methods and procedures of this experiment were designed to adhere as closely as possible to the behavioural paradigm described by Spaak et al. 2014, with a few minor exemptions[3]. Notably, though participants were informed to keep their eyes at fixation, unlike Spaak 2014, eye movements were not recorded during this study and thus trials containing eye movements were not repeated.

[3] We would like to thank Eelke Spaak and Ole Jensen for providing helpful information to assist in this replication effort. We acknowledge all discrepancies in methods noted by these authors in the methods and discussion. The interpretation of the current data is entirely our own.

Furthermore, stimuli were presented on a high-frequency LCD monitor in an office setting, rather than a projection plate in an MEG testing facility. The current methods were as follows (See Figure 4.5):

Participants viewed all stimuli on a 27" ASUS VG278HE LCD monitor with a grey-to-grey response time of 2ms, set to a refresh rate of 60 Hz, normalized to a standard gamma value of 2.2. Participants were seated 60 cm from the screen with their head on a chinrest. Stimuli were presented against a grey back ground (57 cd/m^2) with a white fixation cross (240 cd/m^2, 0.6° diameter) fixed in the centre of the screen. One second after the start of each trial, the priming sequences were presented for 91 frames (1517 ms). The priming sequence consisted of 16 white squares (240 cd/m^2, 6° diameter) presented to the lower left of fixation (centred 6° left and 3° lower), and 16 white squares to the lower right of fixation (centred 6° right and 3° lower). On half of the trials, the squares to the left were presented isochronously (Rhythmic sequence), with an SOA of six frames (100 ms), while the squares to the right were presented anisochronously (Arrhythmic sequence), such that the SOA between each square varied randomly with the constraint of a minimum SOA of two frames and fixed timing of the first and last square to match that of the Rhythmic sequence. On the other half of the trials, the locations of the Rhythmic and Arrhythmic sequence were reversed. Each square was presented for one frame (17 ms). We now refer to the stimulation conditions as Rhythmic and Arrhythmic, rather than Entrained and Non-Entrained, so as to be descriptive of the stimuli presented and agnostic to the entrainment hypothesis in the description of the conditions.

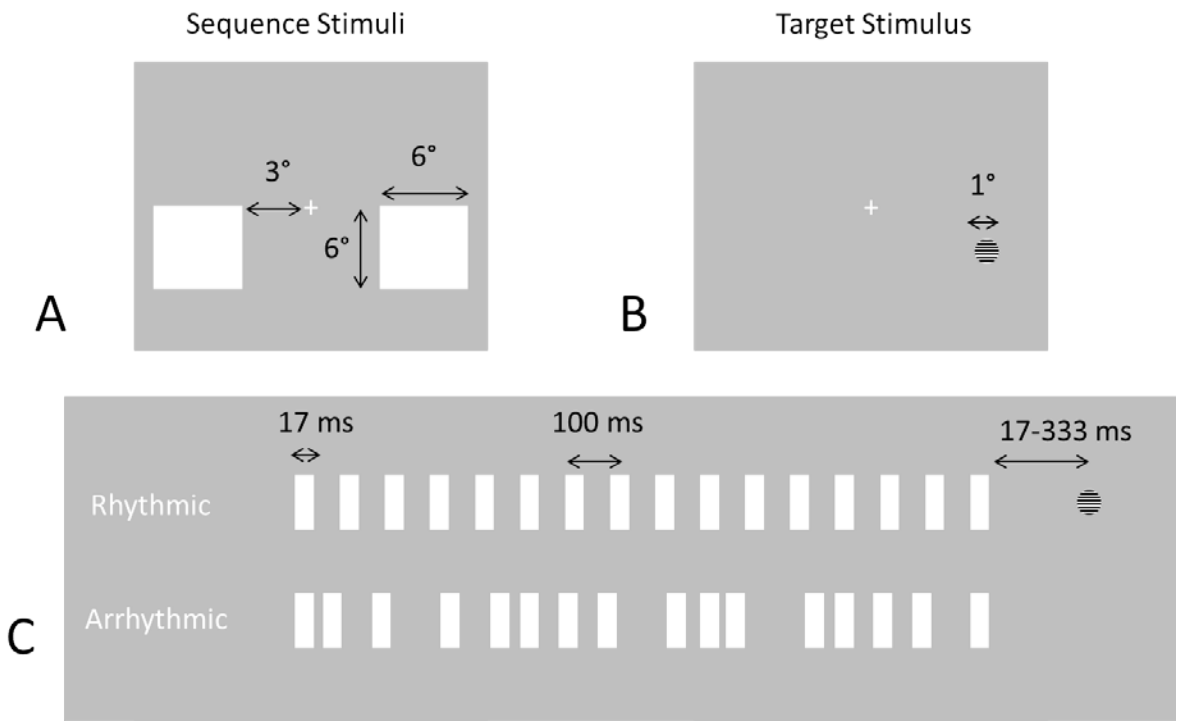

Figure 4.5 Diagrams of the stimuli and trial structure used in Spaak 2014 and the current study. A) White squares were presented to the lower-left and lower-right of fixation B) A low-contrast target stimulus always appeared directly behind the centre of either the left or right white square, counterbalanced C) Exemplar single trial structure. The Rhythmic vs. Arrhythmic sides (left or right) were counterbalanced, as well as the delay of the target from the final white square stimulus (14 possible delays from 17 to 333 ms) and the absence or presence of the target.

After a delay (target delay) of between 1 to 20 frames (17-333 ms ISI), a circular aperture sine wave grating (1° diameter) was presented for one frame (17ms) at the centre of either the lower-left or lower right location of the priming sequence. The participant was instructed to then select the whether the target appeared at the left or right location by pressing the '1' or '2' key on the keyboard, using their right index or middle finger, respectively. After forced-choice response selection, the next trial would begin. No feedback was given.

The main task for each participant consisted of 8 blocks of 80 trials each, for a total of 640 trials. Trial presentation was counterbalanced in a 2x2x20 design (Side of Rhythmicity, Side of Target Presentation, Target Delay), such that each stimulus condition was presented in random order with each block. After each block, participants were forced to take a minimum 30 second break and pressed Enter when they were ready to continue.

Before the main task, participants performed two blocks of a QUEST staircase procedure (Watson & Pelli, 1983), adjusting the contrast of the sign wave within the target stimulus to find the 80% correct response threshold. The first block had only 40 trials and served as a practice block, with the threshold results discarded. The second block had 80 trials and determined the initial sine-wave contrast at the start of the main task. The target contrast in the main task remained fixed within each block, and was updated between blocks to maintain overall 80% accuracy. The overall luminance of the whole target always remained constant, matching the luminance of the background.

Results

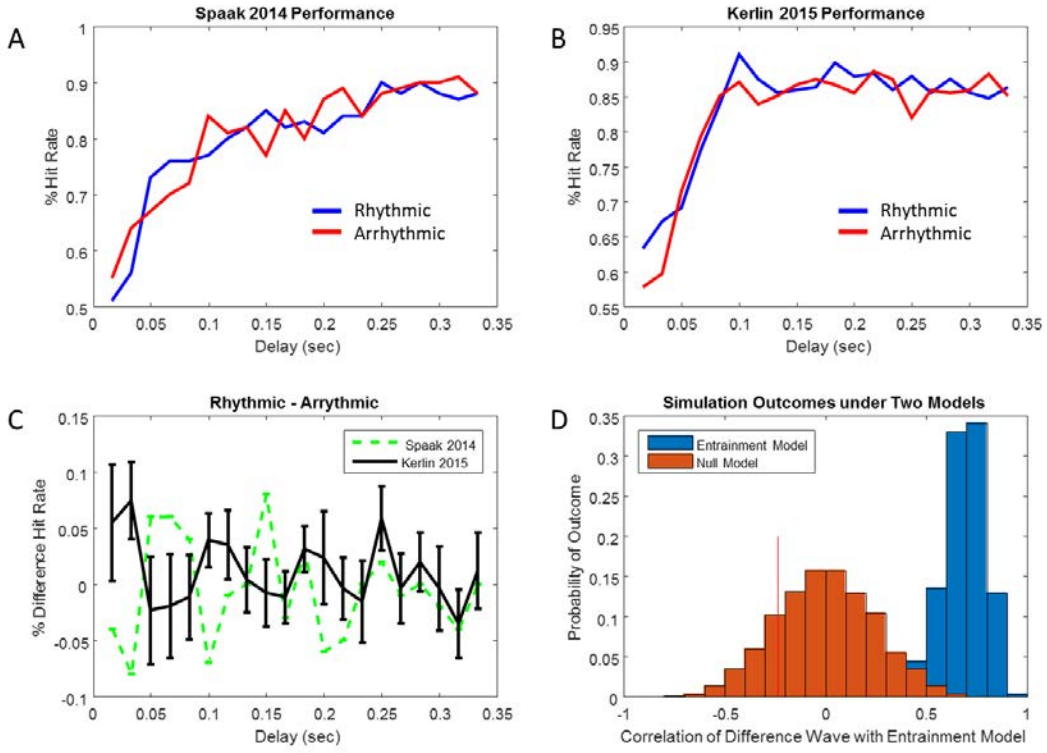

Figure 4.6 Comparison between Spaak 2014 and Kerlin 2015 Results. A: Hit rate across condition Spaak 2014. B: Hit rate across condition Kerlin 2015. C: Rhythmic- Arrhythmic differences across Delay. Error bars for Kerlin 2015 represent standard error. D: Distribution of Pearson correlations between the simulation results and the Entrainment Model. The vertical red line represents the experimentally observed correlation in Kerlin 2015.

As in the previous study, hit rate increased primarily monotonically as a function of Delay in both the Rhythmic and Arrhythmic conditions (See Figure 4.6A,B). However, the primary measure of interest was the difference in hit rate between the Rhythmic and Arrhythmic conditions. As can be seen in Figure 4.6C, the grand averaged difference waveform across delay was substantially different from the model fit to the data of the previous study, hereby referred to as the Entrainment Model ((0.042*sin(10*pi*2*Delay+4.1)). In fact, there was a modestly negatively correlated (Pearson r = -.234) between the observed data and the model. We sought to determine the probability of the current outcome given that the Entrainment Model is true by running a Monte Carlo simulation of the entire experiment. Simulated participants were given a sinusoidal bias in hit rate matching the Entrainment Model, split equally and inversely between the Rhythmic and Arrhythmic conditions. We calculated the Pearson r correlation between the simulated Rhythmic-Arrhythmic grand average difference wave, collapsed for each Delay, and the Entrainment Model for each permutation. Of 1000 permutations tested, none produced a correlation value at or below the current experimentally observed value (See Figure 4.6D, $p < 0.001$). When no entrainment bias was added to 1000 simulations (Null Model), 179 permutations resulted in a correlation value below the experimental observed value ($p = 0.179$). Thus, we failed to replicate behaviour consistent with a fixed-phase response as proposed in the Entrainment Model, and found no evidence to indicate the negative correlation resulted from anything other than random variation.

We then examined whether the observed difference in behaviour demonstrated any evidence of oscillatory activity at 10 Hz. An FFT of the grand average difference wave showed no evidence of a peak in power at 10 Hz relative to surrounding frequencies, suggesting there was no consistent oscillation across participants at 10 Hz (Figure 4.7A). However, if each individual exhibited a 10 Hz behavioural oscillation with a different phase, it would not be observed in the grand averaged waveform. To address this issue, we calculated the FFT of each individual's averaged difference waveform before average FFT magnitude across participants. Again, no peak in power was observed

at 10 Hz (Figure 4.7B), demonstrating the absence of a substantial oscillatory 10 Hz fluctuation in performance at the level of individual participants.

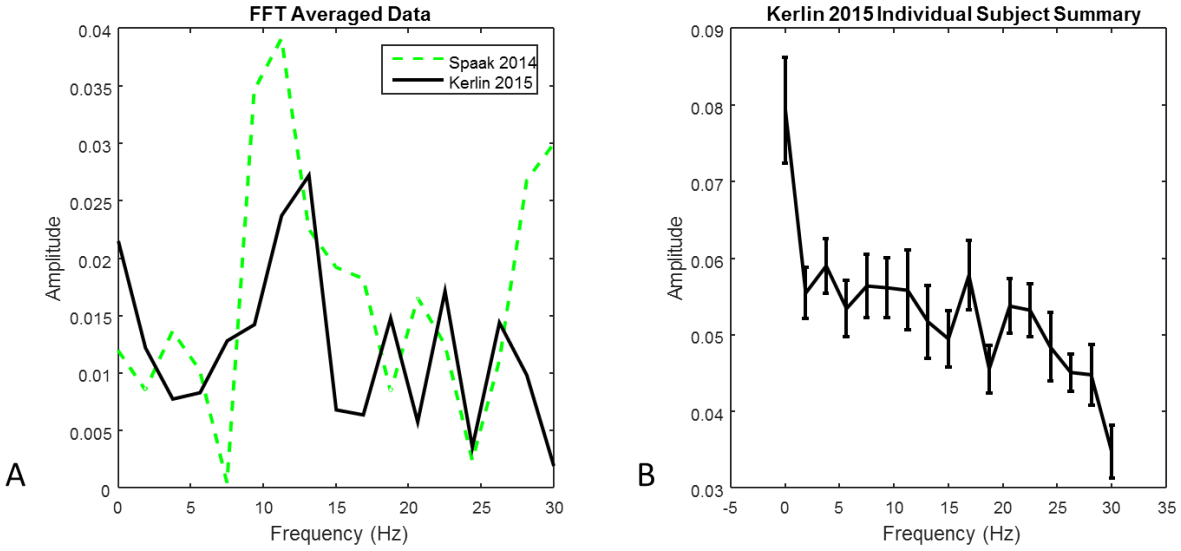

Figure 4.7 Frequency distribution in the behavioural difference waves. A: FFT amplitudes of the grand averaged difference waveforms of Spaak 2014 and Kerlin 2015. B: Average FFT amplitude of the difference waveform of each individual (Kerlin 2015) Error bars represent standard error across participants.

Discussion

The current study attempted to replicate key findings supporting a causal role of alpha entrainment in altering visual target detection through the presentation of rhythmic and arrhythmic visual stimuli, and failed to replicate such supporting evidence. In Experiment 1, we failed to replicate the overall pattern of behaviour observed by Mathewson et al. 2012, finding a monotonic increase in hit rate with increasing target delay following both rhythmic and arrhythmic stimulation, with the notable absence of the substantial drop in hit rate at ~120 ms observed by Mathewson et al. 2012. Examining the difference between the hits and false alarm rates across, we found no evidence of fluctuations in target detection rate matching the RSVP presentation frequency. Overall, hit rate was greater for rhythmic vs arrhythmic stimulation, though this difference corresponded with a similar

shift in false alarm rates, suggesting it is likely driven by a response bias based on the timing of the backward mask, regardless of target presence. In Experiment 2, as in Spaak et al. 2014, we observed a monotonic increase in hit rate accounting for the lion's share of variance in hit rate across delay for both rhythmic and arrhythmic conditions. However, we failed to observe any evidence of an oscillation in hit rate in the difference between conditions at either the level of individual participants or the grand average of all participants, rather, the observed data was significantly inconsistent with the Entrainment Model of Spaak et al 2014. Thus, in two independent cases, we were unable to produce support for frequency matched alpha entrainment of perception using two extant paradigms.

Of course, we must consider known methodological differences between the current experiments and the two previous studies that could account for the discrepancy in results. Firstly, there may have been a critical difference in methodology which prevented consistent oscillatory differences in hit rate from being observed. In Experiment 1, the use of an adaptive paradigm for determining the contrast of the target for each participant could potentially have led to a slight inconsistence in phase and/or an absence of an oscillatory modulation of target perception. If true, this would substantially narrow the conditions in which entrainment is expected to be observed. It is also possible that the increase in the range of target delays in Experiment 1 compared to Mathewson et al. 2012 shifted the locus of temporal attention and therefore performance, though this is unlikely given that a shift in range between Mathewson et al. 2010 and Mathewson et al. 2012 did not lead to a substantially different temporal pattern of results. Experiment 2 was designed to adhere to the original study as closely as possible given our equipment. Though theoretically possible, we do not believe that the lack of an eyetracking control in Experiment 2 was responsible for the discrepancy in our results, as participants were instructed to maintain fixation and the unpredictable, bi-lateral nature of the task afforded no benefit to eye movements prior to target onset, and would have led to poor performance at the contralateral position. Both experiments were conducted in rooms with moderate lighting, though minor differences in reflection and lighting conditions in our laboratory

compared to the MEG bore environment could account for a difference in outcome, though the importance of such factors would narrow boundary conditions under which entrainment in expected to occur.

It is unlikely that our failure to replicate the previous experiments is due to an insufficient number of trials or the level of uncontrolled variance in the current studies. In the case of both Experiments 1 and 2, the total number of trials presented to test the entrainment hypothesis exceeded the total number of comparable trials tested by Mathewson et. al. 2012 and Spaak 2014, respectively. The overall pattern of hit rate across delay is clearly different between studies and outside the margins of error. In Experiment 2, we quantified the likelihood that the true behavioural response pattern matched the entrainment model fit derived from Spaak 2014, given the current data, and found such a result to be extremely unlikely. While we can affirm that we fail to replicate the previous studies, we cannot rule out the possibility that a frequency-matched rhythmic entrainment signal was present and too small to be detected. The current studies were designed primarily to test the replicability of the results of previous studies, which offered clear predictions of the expected magnitude and phase of the behavioural oscillation to be detected as consistent across participants. If entrainment is of inconsistent phase across each participant, given the number of trials collected from each participant in both the current and previous studies, very small fluctuations in hit rate (<5%) would likely be indistinguishable from random error.

To our knowledge, the only other extant study in the literature to provide direct support for the alpha-band entrainment of visual perception is the work of de Graaf and colleagues (de Graaf et al., 2013). De Graaf et. al. 2013 presented annular rings at 3.9, 7.1, 10.6, 14.2 and 17 Hz, followed by a target temporally “in-phase” with the preceding stream, at either the location of the series or a location in the opposite hemifield in a “AFC target identification task (‘+’ vs ‘x’). They found a difference in target identification accuracy when stimuli at 3.9 7.1 and 14.2 Hz were presented in the same vs different hemifield as the target, and so such “cuing benefit” when stimuli were presented

at 10.6 Hz and 17 Hz, regardless of whether or not the rings were changing positions or at a fixed location. In a follow-up experiment, moving annuli were presented at a rate of 10.6 or 5.3 Hz, with target delays varying from 47 to 282 ms. 10 and 5 Hz sinusoidal waveforms were fit to the linearly detrended results of accuracy over time for both conditions, with a 10 Hz fit, and not a 5 Hz fit, explaining a significant amount of the variance in the grand-averaged group data of both conditions. The peak frequency of the behavioural waveform following 10.6 Hz stimulation was positively correlated with the peak frequency of resting state alpha activity. These results, while intriguing, are somewhat difficult to interpret and likely difficult to replicate. Firstly, the effect attributed to entrainment across subjects is exceedingly small, with the amplitude of the 10 Hz best fit no greater than a 1.5% change in hit rate. Since the phase of such a fit was not determined *a priori*, this effect magnitude is likely to be an overestimate. The presence of 10 Hz "power" in the 5.3 Hz condition could be due to the entrainment of alpha by a subharmonic, as the authors propose, though in the absence of a control condition it's possible that a similar non-linear response would occur following any stimulus, particularly if the phase relationship shifts depending on the frequency. Furthermore, the relationship between behavioural frequency and MEG frequency did not have a one-to-one slope and could reflect transient, non-linear changes unrelated to entrainment to the stimulating frequency. However, this correlation is potentially informative regarding the relationship between the inherent speed of perception and the alpha state/trait, to be further addressed in Chapter 5.

The absence of entrainment reported in the current experiment is in stark contrast to the supporting evidence provided in the extant literature. It is possible that the conditions in our lab were uniquely poorly suited for measuring such effects, or that the current experimenter grossly erred in stimulus presentation or analysis in such a manner as to nullify effects which would be present. We find this possibility unlikely, given that each experiment was conducted with different monitors, presentation scripts, and analysis scripts. Anticipated condition specific effects of stimulation, such as forward masking, were clearly present, making a systematic coding error less likely the cause of a spurious null finding. Likewise, there is no evidence to suggest any major systematic error in the

conduct of the experiments in the extant literature. Rather, the discrepancy is likely at least partially accounted for a combination of false positive results due to chance and the multiple comparisons problem, a bias against the publication of null findings (i.e. the file drawer problem) and alternative accounts for non-linear effects on perception. The recent emergence and popularity of the topic of oscillations and entrainment make this outcome particularly likely. Additionally, some of the evidence supporting alpha-band perceptual entrainment may result from changes truly incurred by the phase alignment of endogenous oscillations. If visual alpha-band entrainment does occur, the research community would greatly benefit from entrainment paradigms with objective response measures, sufficient power to test multiple hypotheses, replicated boundary-conditions under which entrainment will or will not occur, and sufficient detail such that the results can be successfully reproduced by the community. As it stands, the small effects previously reported, as well as the absence of any sign of behavioural entrainment in current experiments, demonstrates the remarkable resiliency of the visual system against phase-locking to rapid external stimulation.

Chapter 5: Rhythmic Visual Stimulation and Temporal Perception

Introduction

In Experiment 1 of the previous chapter, we give an alternative account for the findings of Mathewson et al. 2012 with regards to perceptual benefits derived from repeated rhythmic stimulation. We propose that the timing of the repeated masking stimulus, rather than the timing of the near threshold target, accounts for behavioural changes in the likelihood of report of the target, with the detection of temporal anisochrony leading to a shift in criteria towards the report of target presence. This may result from confusion between the detection of changes in timing with the detection of a near-threshold target, with both events leading to the allocation of attention, interpreted as the acquisition of a target in the absence of strong visual evidence. We sought to determine if the reverse conjecture would hold as well; if changes in timing may be confused for the appearance of a near-threshold stimulus, it's possible that changes in the appearance of a series of objects would alter the perception of near-threshold changes in timing.

There are a number of previous studies which have examined the role of object change on subjective duration. For instance, it is known that the initial item in a series of items tends to have a much longer perceived duration than subsequent identical items (Kanai & Watanabe, 2006) and novel objects appear to have longer subjective durations than standards when presented within a series of repeated objects (Pariyadath & Eagleman, 2007; Tse, Intriligator, Rivest, & Cavanagh, 2004). The subjective time dilation of changing stimuli may be due to a direct relationship between the amount of neural processing evoked by an item and the object's subjective duration, as both object size and intensity are known to be associated with subjective duration (Xuan, Zhang, Chen, He, & Chen, 2007). While it is well established that object change results in greater subjective durations, to our knowledge, there is little evidence as to whether visual object change alters the ability to detect

changes in interval timing. Determining the effect of object change on temporal perception could also serve to elucidate how high-speed visual temporal judgements are encoded in the brain.

In previous chapters, we have discussed how the rhythmic entrainment of endogenous oscillations has been proposed as a mechanism leading to frequency-matched fluctuations in the attentional blink, perceptual discrimination (de Graaf et al., 2013) and near-threshold detection (Mathewson et al., 2010; Spaak et al., 2014), finding no evidence in support of the hypothesis and substantial evidence for alternative accounts of previous findings. Meanwhile, the rhythmic entrainment hypothesis has not only been proposed to account for biases in the perceptual selection of targets, but also in the judgement of the timing of individual items within a rapidly presented series. Barnes and Jones propose an influential model regarding the role of oscillations on temporal interval judgements, based on experiments in the auditory domain (Jones et al., 2000). Under this version of the rhythmic entrainment model, the dynamic attending model, each successive presentation of an item in an RSVP series drives a frequency-matched oscillator, increasing the amplitude of the oscillator, which in turn results in matching fluctuations in attentional focus. These fluctuations then result in an enhanced ability to detect changes in interval timing during or following isochronous sequences. The phase of the oscillator at the time of an item's onset serves as a code for whether an item occurred earlier or later than expected. This model of temporal irregularity detection predicts that greater phase locking at the stimulation frequency will lead to more accurate detection of temporal anisochrony.

Alternatively, the detection of fine changes in temporal onset within a rapid series may be better explained by a local, state dependent model of time perception (Buonomano & Merzenich, 1995; Karmarkar & Buonomano, 2007). Local state based models do not depend on a frequency-matched temporal oscillation for temporal judgements, but rather predict that timing information is extracted by reading out the complex firing state of the relevant neural system given natural neural response dynamics at multiple timescales. This model predicts that any neural response inconsistency caused

by temporal unpredictability immediately prior to the test interval will result in less precise temporal judgements. Karmarkar & Buonomano conducted a series of experiments that supported this conclusion, finding that temporal discrimination was disrupted by variability in the preceding interval for short (100 ms) but not long (1000ms) intervals between auditory tones (Karmarkar & Buonomano, 2007), and that behavioural performance could be produced by a neurophysiologically plausible neural network model. However, it is unclear whether similar results would be found in the visual system.

We hypothesized that changes in object shape would lead to deficits in the detection of relative changes in timing at faster rates of stimulus presentation due to the masking of subtle, local neural state changes required for temporal interval judgements at high speeds of presentation. Alternatively, if alpha-band specific entrainment provides a more robust or precise visual temporal coding, we would expect greater temporal precision when items and presented at alpha-band rates regardless of changes in object shape, as both repeated and changing objects presented in the alpha-band would produce substantial phase-locked alpha activity.

Experiment 1

In Experiment 1, we asked participants to report whether a series of objects contained temporal irregularity, with half of trials consisting of the repetition of a single letter (Repeated Condition), and the other half a series of letters with changing identity (Changing Condition). We presented the letters for each condition at 4 different speeds: 3 Hz, 6 Hz, 12 Hz, and 24 Hz. If changes in object shape disturb changes in the perception of relative timing, we would expect to see more false alarms and/or misses during Changing trials than Repeated trials, particularly at faster rates of presentation (> 6 Hz). If alpha-band entrainment provides superior temporal coding, we expect more hits and

fewer false alarms during both the Changing and Repeated conditions at 12 Hz, relative to surrounding frequencies.

Methods

Fourteen participants (mean age: 20.1 years, 11 female, 3 male) took part in Experiment 1. All participants reported normal or corrected-to-normal vision.

All stimuli were presented on an ASUS VG278HE 27“ LCD monitor with a grey-to-grey response time of 2ms, set to a refresh rate of 144 Hz. Participants were seated ~70 cm from the centre of the screen. The stimuli for each trial consisted of the serial presentation of nine black letters (Arial Bold 36 point font, ~1° visual angle) presented at the centre of the screen for one frame (7 ms) each on a grey (36 cd/m^2) background (See Figure 5.1). For the Changing Identity condition, each successive letter within a trial was randomly selected without replacement from any of the 26 letters of the English alphabet. For the Repeated Identity condition, a single letter was randomly selected and repeated nine times. The letters were presented at one of four different rates (Frequency): 3 Hz, 6 Hz, 12 Hz or 24 Hz, corresponding to fixed SOAs of 333 ms, 167 ms, 83 ms, and 42 ms, respectively, for isochronous (Regular) trials. For anisochronous (Irregular) trials, four of eight randomly selected SOAs between letters would be shortened, and the other four lengthened, by an amount determined by the Jitter condition; a 17%, 33%, 50%, 67% or 83% change relative to the isochronous SOA matching the trial Frequency. This ensured that the first and last letter of the sequence were presented at the exact same time as the Regular sequence on every trial. For the main experiment, each Frequency condition was blocked within participants and the Frequency order was counterbalanced across participants using a random Latin square design, with 240 trials per frequency per participant. For half of participants, the first 120 trials of each frequency were the Changing Letter condition, and the last 120 trials were the Repeated Letter condition. For the other

half of participants, this order was reversed. Participants were given a minimum 30 seconds break every 120 trials. Thus each Frequency (3 Hz, 6 Hz, 12 Hz, 24 Hz) x Identity (Repeated, Changing) combination was tested in eight separate blocks. Within each block, half of trials were Regular and half Irregular, in random order. The five Jitter conditions were randomly counterbalanced across all Irregular trials within a block, resulting in 12 trials of each Jitter condition in each block.

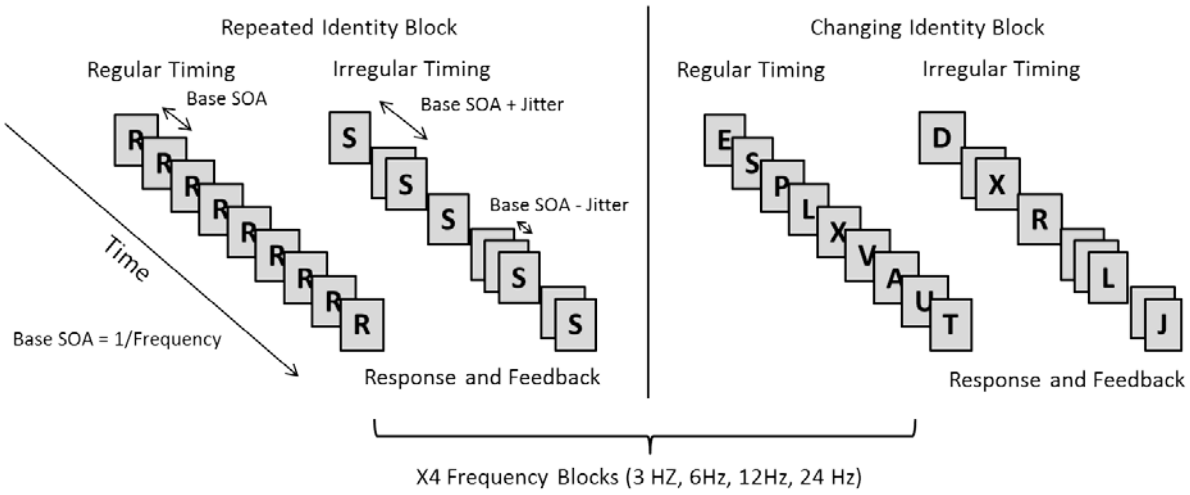

Figure 5.1 Experiment 1 trial structure. The participant's task for each trial was to determine whether the presented sequence was temporally Regular or Irregular, ignoring letter identity. Letter Identity and Frequency conditions were blocked. Regular and Irregular trials were randomly mixed.

A trial began with 500 ms of a blank grey screen, followed by the nine-letter sequence, and a final blank screen. Participants were instructed to make a response immediately after the end of this sequence. The participants' task was to determine whether the timing of a trial sequence was regular or irregular, regardless of whether the identity of the letters changed, by pressing keyboard buttons '1' or '2', respectively, with their right hand.

If the response was correct, a 440 Hz auditory beep was presented as immediate feedback through a set of headphones. If the answer was incorrect, no beep was presented. Participants were informed

they would receive 10 points for each beep (correct answer), and to try to maximize the number of points received based on feedback (no particular reward was promised or given).

After each block, participants were presented with the score earned for that block, as well as their total score. Before the start of each new block, participants were presented with the words "New Trial Type!" for five seconds to remind participants of the change in Frequency and/or Identity conditions between blocks.

Before the main experiment, participants performed a practice session. For the practice session, all Irregular trials were set to the largest Jitter condition (83% jitter) and 10 irregular and 10 regular trials were presented for each Frequency x Identity block, for a total of 160 trials. The Frequency x Identity block order was the same for the practice session as for the main session, except no breaks were given between blocks. Auditory feedback, point structure, and task instructions were identical to the main experiments.

Analysis

Hit rate, false alarm rate and D-prime were calculated for each participant and each condition, collapsed across Jitter magnitude, with hits defined as the correct detection of an irregular trial. Prior to calculating D-prime, hit rates and false alarm rates of 1 or 0 were adjusted to .99 and .01, respectively, in order to reflect the finite number of trials tested in each bin and avoid infinite D-prime values. D-prime values, reflecting shifts in signal detectability regardless of shifts in report criteria, was used as the dependent measure in a two-way 4 (Frequency) x 2 (Identity) repeated measures ANOVA.

Results

As can be seen in Figure 5.2, D-prime was sustained at all four frequencies in the Repeated condition, implying that the ability to detect changes in timing is approximately constant as a fraction of the inter-item interval (i.e. the Weber fraction) over a wide range of frequencies. However, in the Changing condition, performance dropped substantially at frequencies above 6 Hz, within decreasing hit rate and increasing false alarm rate, suggesting that changes in object shape incurs a breakdown in temporal interval processing at high speeds (> 6 Hz). This description is supported by statistical analysis. A two-way ANOVA of d-prime revealed main effects of both Letter Identity ($F(1,39)$ = 11.5, p = 0.005) and Frequency ($F(3,39)$ = 13.2, p < 0.001), as well as an interaction ($F(3,39)$ = 7.9, p < 0.001). A one-way ANOVA across Frequency for the Repeated condition demonstrated no significant effect of Frequency on D-prime ($F(3,39)$ = 1.76, p = 0.172), whereas D-prime depended heavily on Frequency in the Changing condition ($F(3,39)$ = 23.37, p < 0.001). Finally, paired t-test comparisons of D-prime between the two Letter Identities (Changing vs Repeated) for each Frequency showed significant differences at 12 Hz (p = 0.017) and 24 Hz (p < 0.001), with greater sensitivity for Repeated than Changing, though no significant differences in Letter Identities were observed at 3 Hz (p = 0.88) and 6 Hz (p = .99).

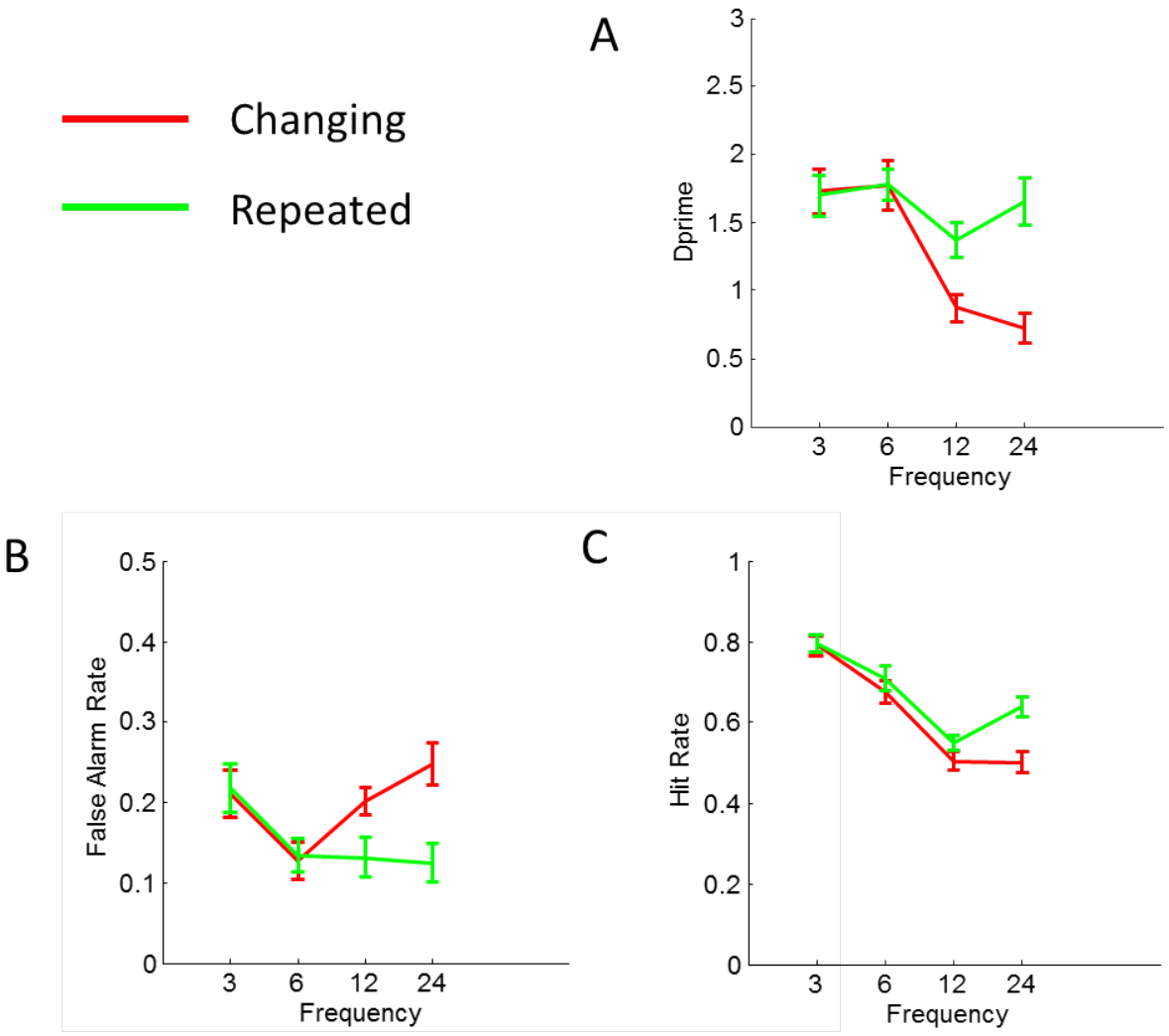

Figure 5.2 Anisochrony detection performance for each Frequency by Condition. Line plots show average participant A) D-prime, B) False Alarm Rate, and C) Hit rate. Error bars represent between subject standard error from the mean.

Thus, changes in object shape result in a substantial disruption of visual perceptual interval timing at high temporal frequencies. This disruption is reflected in both increases in the false perception of irregularity during rapid, regular stimulation (increased false alarms) and the inability to detect irregularity during irregular stimulation (reduced hit rate). This difference in perceptual performance was not restricted to the alpha-band frequency (12 Hz), but rather increased from 12 to 24 Hz, inconsistent with the alpha-band entrainment hypothesis. However, it remains unclear as to the root cause of the cost of letter change on temporal change discrimination.

Experiment 2

In Experiment 1, we established a deficient in detecting changes in rapid interval timing with concurrent changes in object shape. Changes in object shape could adversely impact temporal change detection by introducing variability in the time to process of each item, resulting in an inability to precisely compare the arrival times of each object. This imprecision could, in turn, disrupt frequency-matched entrainment, leading to poorer temporal acuity. In Experiment 2, we sought to test this account by comparing anisochrony detection ability when temporal changes occur near the beginning compared to near the end of the stream under Changing and Repeated conditions. If rapid temporal change detection relies on frequency-matched entrainment by a repeated RSVP, we would expect substantially enhanced performance at detecting temporal changes near the end of the series, particularly in the Repeated condition. In addition, we measured EEG activity during an anisochrony detection task with Changing and Repeated letters. If changes in object shape result in increased variability in the timing of item processing, we would expect to see a reduction in stimulus phase-locked activity in the Changing condition relative to the Repeated condition. However, if changes in object shape produce activity with precise timing and increased activation, we would expect to see an increase in stimulus phase-locked activity in the Changing condition compared to the Repeated condition.

Finally, we sought to determine whether the visual system is more or less sensitive in detecting single short (e.g., SOA is 80 ms when base SOA is 100 ms) or long (e.g., SOA 120 ms when base SOA is 100 ms) intervals relative to fixed (e.g., ISO is always 100 ms) intervals in a series. If high-speed temporal change detection is based upon frequency-matched entrainment with predicative phase coding, we would expect to see equal or greater sensitivity to short intervals relative to long intervals, as phase-locked activity will either be maintained or decay over time. If high-speed temporal change detection is more reliant on detecting late onsets (i.e. gap detection), we would

expect the opposite result (See Figure 5.3a). For Irregular trials in Experiment 2, we moved a single item forward in time in order to imbed a short interval followed by a long interval (Advanced trials) or delayed a single item to imbed a long interval followed by a short interval (Delayed trials) in the otherwise regular RSVP stream. To establish whether the long or short interval is used for detection, we examined the P3b ERP component, a well-established neurophysiological marker of sensory target detection, measured as voltage increase ~300 following target detection (Comerchero & Polich, 1999). We predicted earlier irregularity detection, as indexed by the latency of the P3b component, on Delayed trials compared to Advanced trials if participants are better at detecting long intervals than short intervals in the context of a high-speed RSVP series.

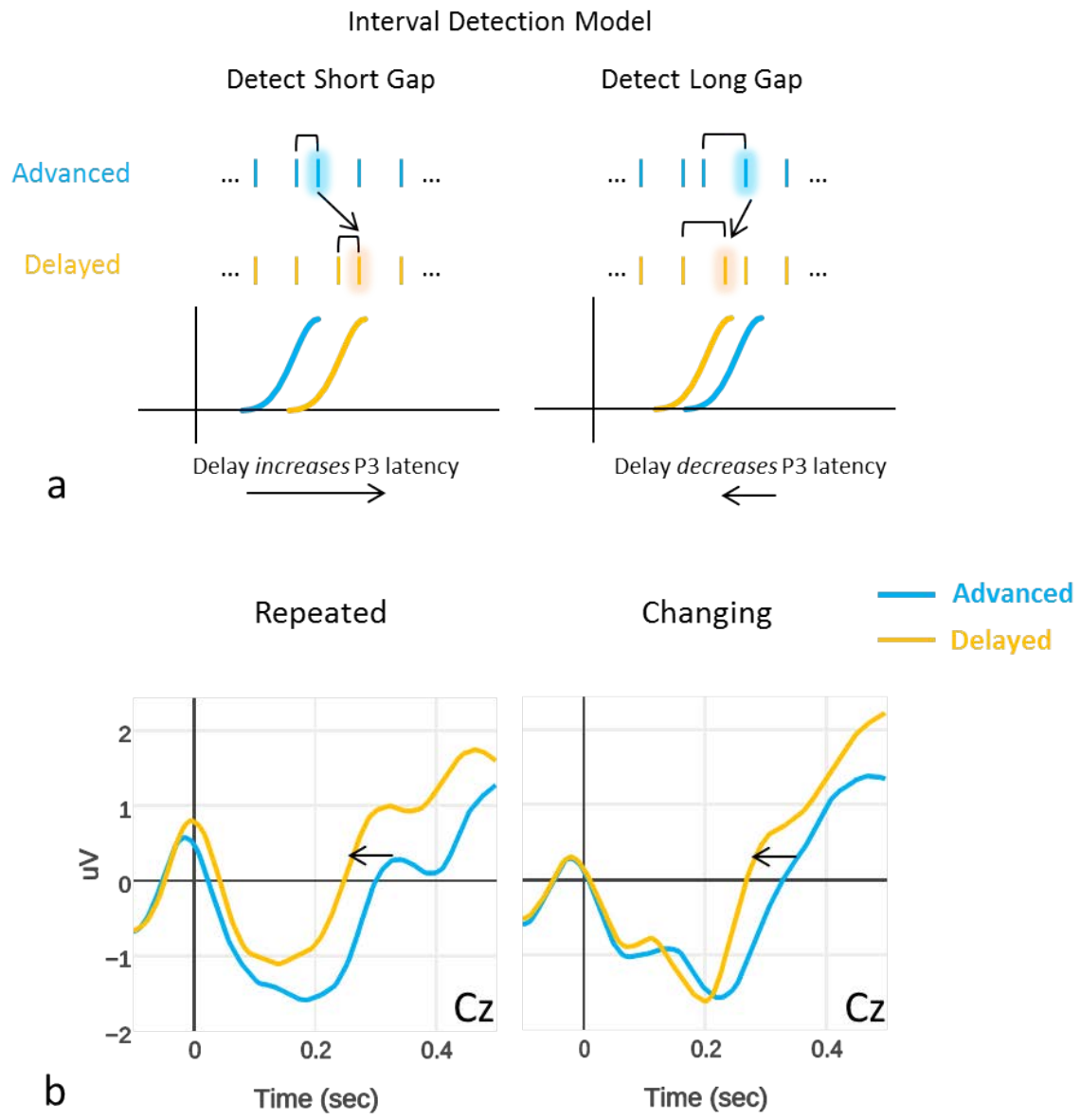

Figure 5.3 Interval detection model and results. a) A schematic of the Short and Long Interval detection models and experimental predictions. b) ERPs of following detected targets (3rd position and 10th position collapsed). Zero point corresponds to the expected onset of the probe item. The earlier P3 latency observed under the Delayed condition supports hypothesis that anisochrony detection is more reliant on gap detection than early onset detection at equal anisochronies in both the Repeated and Changing conditions.

Methods

Thirty-one participants (mean age: 21.2 years, 21 female, 10 male) took part in Experiment 2. Potential participants were presented with a lab standard questionnaire, and only qualified individuals were allowed to participate in Experiment 2 (See Appendix B).

Participants were to be excluded from the main task if the total score for the thresholding session (See Thresholding procedure) was negative, indicating a poor threshold estimate (3 excluded) or more than 25% of EEG trials in the main session were artefact rejected (Sawaki & Luck, 2010) (2 excluded). EEG data could not be collected due to technical issues in an additional two participants. Thus, only the remaining twenty-four participants were included for all analyses.

For the Regular condition in Experiment 2, twelve letters, either Repeated or Changing, were presented at a single frequency (10.3 Hz, 97 ms SOA). For the Irregular condition, either the third letter or the tenth was shifted either forward (Advanced) or backward (Delayed) in time relative to isochronous timing (See Figure 5.4). The magnitude of this temporal shift was determined by the Anisochrony Magnitude of a given trial (See Thresholding procedure). The total sequence length remaining fixed at 1174 ms across all trials. Anisochrony Position (3^{rd} or 10^{th}) was manipulated in a blocked design, alternating between 3^{rd} and 10^{th} between each block, with the initial block type counterbalanced between participants. Participants were instructed to determine whether a letter was “in-sync” or “out-of-sync” each trial, by pressing the ‘1’ or ‘2’ key on the numpad, respectively. Before the beginning of each block, participants were informed which letter (the 3^{rd} letter or the 10^{th} letter) would potentially change position. Trials of each Temporal Regularity condition (Regular and Irregular) and Anisochrony Direction (Advanced and Delayed) were randomly distributed within a block in the following fixed proportions: 50% Regular, 25% Irregular Advanced, and 25% Irregular Delayed.

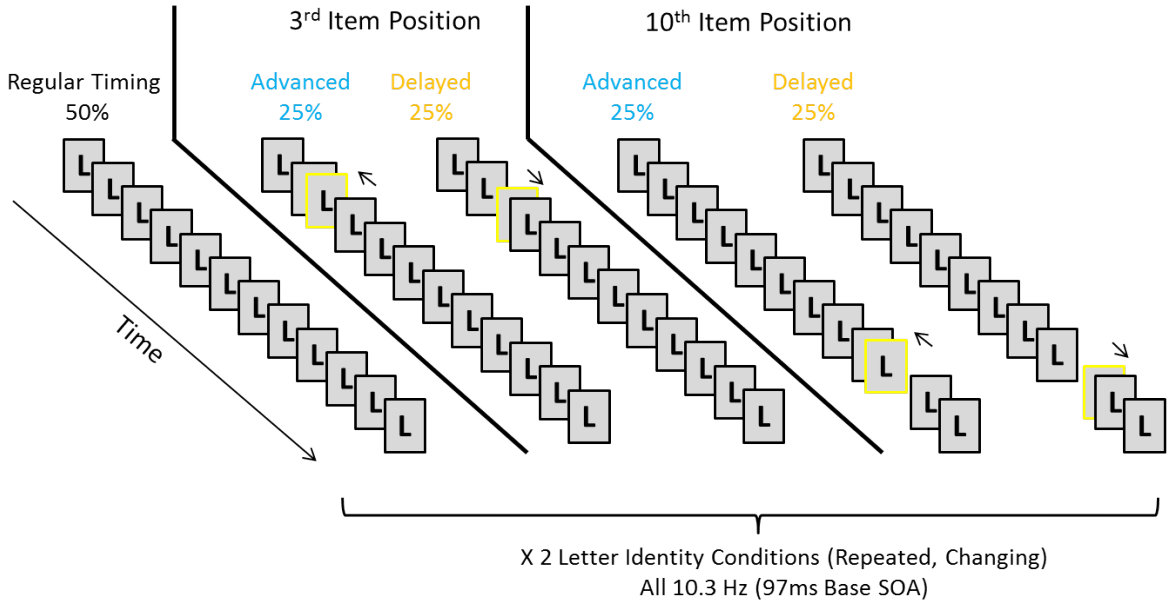

Figure 5.4 Experiment 2 trial structure. Changes in timing were produced by shifting the temporal position of either the 3rd or 10th item. The temporal position of all other items relative to the first item remained constant. In Advanced trials, the temporal irregularity was a short SOA followed by a long SOA. For Delayed trials, the irregularity was a long SOA followed by a short SOA.

To ensure that hits substantially exceeded false alarms for each participant, the following information and incentive procedure was chosen: Participants were informed they would earn 10 points for successfully detecting an "out-of-sync" letter (a hit), but would lose 20 points for reporting "out-of-sync" when the relevant letter was actually "in-sync" (a false alarm). In practice and thresholding sessions, participants were given auditory feedback immediately after making an "out-of-sync" response: a 1000 Hz "high" tone after a hit, and a 200 Hz "low" tone after a false alarm. For "in-sync" responses (misses and correct rejections), no feedback was given and no points were given or deducted. No auditory feedback was given in the main session. Participants were informed in advance that half of trials would in "in-sync" and half "out-of-sync". After each block, participants were given a summary including the number of points earned from hits, the number of points deducted for false alarms, the corresponding score for the block (hit points minus false alarm points), and the aggregate score across all blocks. As in Experiment 1, participants were asked to maximize their score, though no reward was promised or given.

Participants completed two blocks with 20 trials each in a practice session (40 trials), followed by four blocks of 40 trials in the thresholding session (160 trials) and 12 blocks of 40 trials in the Main session (960 trials). The block feedback summary was held on the screen for 30 seconds, after which participants were instructed to press Enter when they were ready to begin the next block (self-paced). A longer (5-10 minute) break was encouraged after six blocks of the main task.

Thresholding procedure

Before the main session, participants performed a thresholding session to approximately determine the temporal change required to produce an "out-of-sync" successful detection rate of 50% using the Bayesian QUEST adaptive staircase procedure (Watson & Pelli, 1983) with an initial estimated Anisochrony Threshold (deviation from a 97 ms "in-sync" SOA) of 50 ms (beta = 3, delta = 0.01, gamma = 0.15). The thresholding procedure was applied independently for each combination of Letter Position (3^{rd} and 10^{th}) and Identity (Changing and Repeated), to produce four separate Anisochrony Thresholds. After the thresholding session, the gamma value of the QUEST procedure, representing the estimated false alarm rate, was changed to match the actual false alarm rate of each of the four separate conditions (3^{rd} Changing, 3^{rd} Repeated, 10^{th} Changing, 10^{th} Repeated) during the thresholding session. If no false alarms were made within a condition (0% false alarm rate), the gamma value was set to 0.0125 (1.25% estimated false alarm rate). The final Anisochrony Detection Threshold for each condition was then recalculated using this gamma value and used as the fixed Anisochrony Magnitude for each condition for each participant in the main session.

EEG Recording

EEG head cap and electrode placement occurred following the thresholding session. EEG was recorded using a BioSemi ActiveTwo system with active Ag/AgCl electrodes connected with conductive gel. A custom head cap (Sawaki & Luck, 2010) was used to collect EEG data from 32

additional sites, with greater density over the occipital lobe (Fp1, Fp2, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P9, P7, P5, P3, P1, Pz, P2, P4, P6, P8, P10, PO7, PO3, POz, PO4, PO8, O1, Oz, O2, and Iz). EEG recordings were also taken from the left and right mastoid, and electrooculogram (EOG) recordings were taken to the left and right of each eye (HEOG) and above and below the right eye (VEOG). All signals were recorded unfiltered at a rate of 2048 Hz, down-sampled offline to a rate of 256 Hz. Before the main session, three short (60 second each) recording sessions were collected, with the stimulus presentation display turned off. In an Eyes Closed session, participants were asked to sit still with their eyes closed for 60 seconds while EEG was recorded; an Eyes Open session looking at the centre of the blank display. In an Artefact session, participants were repeatedly asked to blink, move their eyes left, right, up, and down, and clench their teeth to produce the most common EEG artefacts. This was followed by the main behavioural session, during which EEG was continuously recorded, with triggers sent to the EEG host computer to record the onset of the stimulus sequence in each trial (960 events).

Behavioural Analysis

A two-way (Letter Identity X Position) repeated measures ANOVA was performed, with each individual's final Anisochrony Detection Threshold (ADT) as the dependent measure.

Phase-locked Time-Frequency Analysis

All phase-locked time frequency analysis was performed in FieldTrip (Oostenveld, Fries, Maris, & Schoffelen, 2011). Each EEG trial was epoched from 200 ms prestimulus to 1200 ms poststimulus, and filtered with a 30 Hz first order Butterworth low-pass filter after mean removal and re-referencing to the average of all 32 electrodes. All trials in which any channel exceeded a range of +-100 uV, bipolar VEOG and HEOG activity exceeded 80 uV were rejected. Phase-locked activity during Regular stimulation was compared between the Changing and Repeated conditions by time-lock averaging all Regular non-artefact trials for each Letter Identity condition, collapsing across all other

factors. Time-frequency spectrograms were calculated from the averaged waveforms of each channel of each participant via a 3-cycle Morlet wavelet transformation, with the frequency ranging from 4 to 20 Hz with 2 Hz increments, measured from 0 to 1000 ms with 100ms intervals. Time-frequency-channel clusters were identified based on the difference spectrograms of the Changing minus the Repeated condition via non-parametric cluster selection accounting for spatial, temporal and frequency proximity (cluster alpha threshold = 0.05). Clusters were tested for statistical significance by comparing the empirical results to a Monte-Carlo simulation of 1000 permutations of cluster activity with shuffled condition labels across all 24 participants (significance alpha threshold = 0.05), as implemented in FieldTrip.

Advanced vs Delayed P3 Analysis

The EEG data for each trial was epoched from 300 ms before to 500 ms following the Regular (expected) onset time of 3rd Item (194 ms after first stimulus onset) or 10th Item (875 ms after first stimulus onset), for the 3rd Position and 10th Position conditions, respectively. The EEG data was referenced to the average of all 32 electrodes and baseline centred from -200 to 0 ms. All epochs in which the voltage of any scalp electrode exceeded a range +-100 μV were rejected from further analysis. Bipolar HEOG and VEOG montages were used to screen for horizontal eye movement and blinks, respectively, each with a rejection threshold range of +- 80 μV. Participants were not included for further ERP analysis if the number of correct, non-rejected trials fell below 5 in any of the eight conditions. Correct trials were then averaged into 4 bins (Identity(2) x Probe Direction(2)), collapsing across Item Position and participant, and smoothed with a moving average of 100ms. The grand average peak amplitude at Cz for each condition was measured as the maximum averaged ERP value with a 200 to 500 ms post expected onset time window. The P3 latency was measured as the time point at which half the peak amplitude was exceeded.

Results

As can be seen in Figure 5.5, a large difference in Anisochrony Detection Thresholds were observed between the Repeated and Changing conditions ($F(1,23)$ = 53.4, p < 0.001), with much lower thresholds (i.e. better detection performance) in the Repeated condition than the Changing condition, replicating the pattern observed at the 12 and 24 Hz frequencies in Experiment 1. A modest difference was also observed between item Positions ($F(1,23)$ = 6.90, p < 0.015), with better temporal change detection at the 10th item position than the 3rd position. However, no significant interaction was observed between Letter Identity and Position ($F(1,23)$ = 1.94, p < 0.177), suggesting that while extended RSVP presentation may benefit temporal change detection, the relative benefit of the Repeated condition does not rely on a long series of rhythmic entrainment.

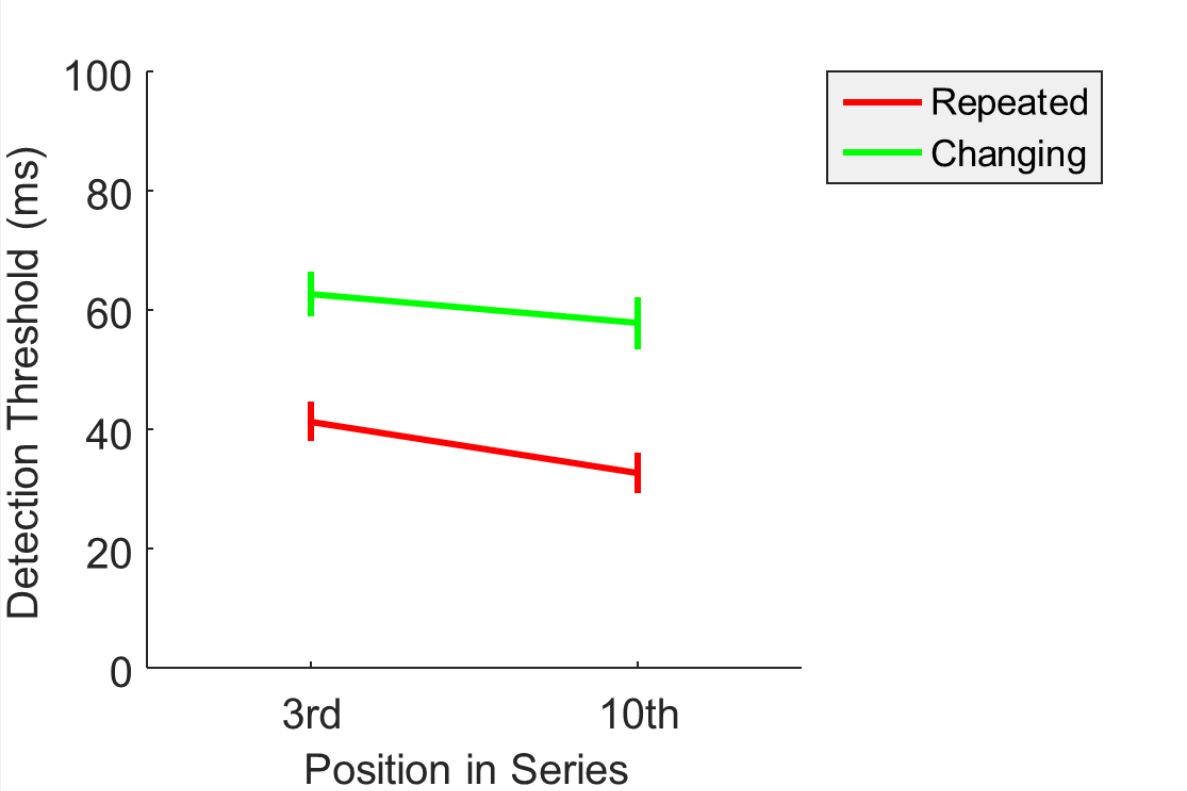

Figure 5.5 50% Detection threshold estimates by Position and Letter Identity. Error bars represent standard error from the mean.

If changing object identity adversely affected the precision in the timing of phase-locked activity, we expected a decrease in phase-locked activity for the Changing condition compared to the Repeated condition. Instead, we found the opposite pattern, with a significant cluster of greater alpha-band, phase locked activity in the Changing condition than the Repeated condition (p = 0.001)(See Figure 5.6). This positive cluster was spatially distributed with an anterior/posterior topography consistent with a source or multiple sources originating in occipital and/or parietal cortex, with a possible contribution from frontal sources. Early (~300 ms after first-item onset) increases in change related phase-locked activity were most strongly observed at lateral parietal electrodes, whereas later (300-1000 ms) increases were distributed throughout posterior and anterior electrodes. No significant negative (Repeated > Change) clusters were observed. Thus, contrary to the hypothesis that phase-

locked entrainment enhances temporal precision, the condition with poorer behavioural temporal precision produced greater phase-locked activity at the frequency of stimulation.

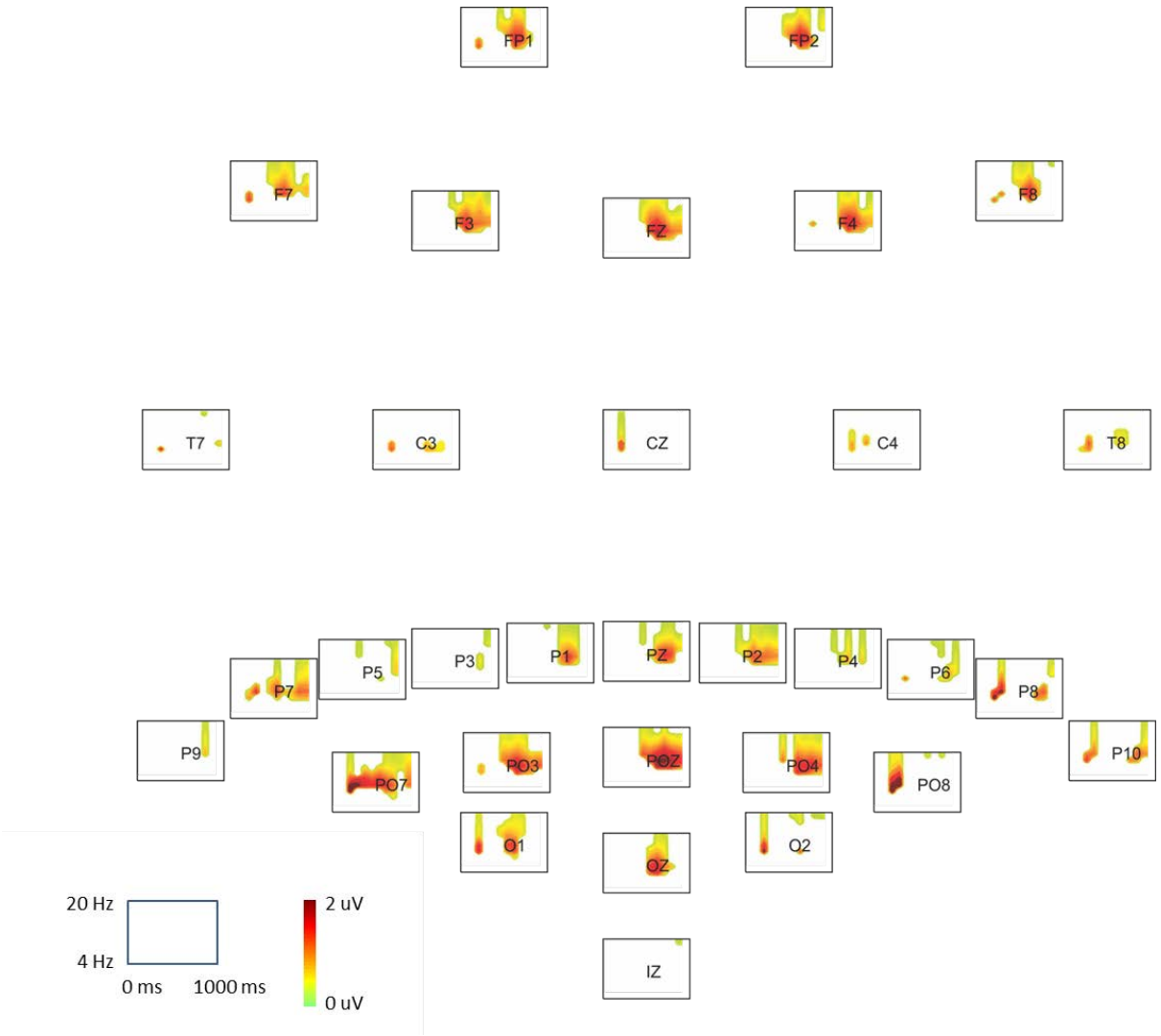

Figure 5.6 Topographic spectrograms of the difference in the frequency characteristics of within-subject grand averaged activity between Changing and Repeated conditions when no anisochrony is present (Regular condition). Results are masked to present the only significant cluster (p = .001), showing greater phase-locked alpha-band activity during the Changing condition than the Repeated condition. The topography is consistent with occipital and/or parietal sources.

Sinusoidal entrainment, phase-coding models of anisochrony detection predict equal or greater sensitivity to shortened (Advanced) vs lengthened (Delayed) intervals, as each will be equally distant in phase relative to the entrained phase, assuming the precision of phase coding is constant or decays over time. This would lead to an earlier P3b onset for Advanced vs Delayed anisochrony trials (Figure 5.3a). Instead, we found a significantly earlier P3b onset in response to Delayed anisochrony trials, suggesting that participants were relying primarily on long intervals for the detection of anisochrony in the series. This was evident in both the Repeated (p = 0.005) and Changing (p = 0.008) conditions (Figure 5.3b).

Discussion

We sought to determine whether temporal interval change detection during RSVP is disrupted or enhanced by changes in object shape and, if so, whether such changes could be attributed to changes in visual entrainment. In Experiment 1, we found that changes in letter identity during an RSVP stream reduced individuals' ability to detect temporal irregularities at presentation rates above 6 Hz. In Experiment 2, we tested whether the deficit in temporal interval change sensitivity caused by object change is due to a loss of phase-locked, stimulus driven oscillatory activity produced by an extended period of repeated rhythmic stimulation. Instead, we found that the detriment of object change on temporal change detection did not rely on extended rhythmic stimulation, object change enhanced rather than reduced rhythmic entrainment, and participants were more sensitive to lengthened intervals than shorter intervals. These results suggest that rhythmic entrainment is a poor fit for explaining rapid temporal change detection and its sensitivity to serial object continuity.

Rather, we propose that the most sensitive form of temporal change detection during rapid object RSVP relies on local spatiotopic processing in the occipital/parietal lobe that simultaneously codes

for ‘what’, ‘where’ and ‘when’ (Burr, Tozzi, & Morrone, 2007). The finest sensitivity to temporal change may not rely on explicit coding of temporal intervals, but rather the capture of attention in response to a local state change in activation that is not attributed to a change in position, contrast or shape. When individuals are presented with a series of changing objects, the onset of new objects triggers obligatory visual activation lasting over 150 ms post onset, masking subtle changes in local activation patterns produced by modest changes in relative timing. This masking activation induced by object change decays over time, resulting the better detection of lengthened intervals (“gaps”) than shortened intervals. Illusory perceptions of changes in timing during isochronous presentation can occur when neural state changes triggered by the onset of new objects are misattributed to temporal irregularity, resulting in a “false alarm” sense of temporal change. Meanwhile, changes in timing are missed when they are falsely attributed to changes induced by new object appearance.

The proposed framework accounts for both the behavioural and neurophysiological findings of the current set of experiments. However, alternative accounts and caveats should be considered. The current experiments cannot entirely rule out a role for rhythmic entrainment in temporal anisochrony detection. For instance, while we measured phase-locked activity at the scalp with EEG as our best estimate of stimulus-driven oscillatory neural activity, it remains possible that this activity is masking a smaller, focally entrained oscillation with greater phase-locked activity to repeated than changing stimuli, responsible for enhanced temporal precision. However, such an entrainment model would still fail to account for the enhanced detection of lengthened vs shortened intervals. Nevertheless, the absence of entrainment as the primary mechanism of rapid anisochrony detection does not rule out a role for oscillations in temporal resolution. In particular, two recent studies reported correlations between the an individual’s ongoing alpha frequency and behaviour, with higher alpha frequencies leading to finer temporal discrimination between of two visual objects (Samaha, Postle, et al., 2015) and greater susceptibility to audio-visual illusion at shorter intervals (Cecere et al., 2014). The latter study also found that the auditory temporal separation required illusory visual perception could be shortened or lengthened by tACS stimulation

at frequencies just above or below the IAF, respectively. However, it remains unknown whether such effects of tACS are due to entrainment, or other indirect physiological responses to stimulation at different frequencies (Helfrich et al., 2014a; Vossen, Gross, & Thut, 2014).

The current result does not exclude a link between the frequency of endogenous alpha activity and the resolution of temporal perception. Rather, it provides evidence that regional entrainment of such oscillations to the frequency of visual stimulation is not the mechanism by which temporal isochrony judgements are made. We instead propose that object change disrupts the detection of temporal change by overwriting and masking less robust temporal change signals while processing new objects.

Chapter 6: General Discussion

A number of empirical investigations and reviews have proposed that endogenous brain rhythms lock to the phase and frequency of external rhythms, serving as a critical mechanism for experiencing the world perceptually. Recently, it has been proposed that 8-12 Hz alpha-band activity plays a critical role in selecting and segmenting visual information, and that this functional role and its consequences may be reliably driven by frequency-matched external visual stimulation. We investigated whether rhythmic visual stimulation led to enhancements or reductions in visual perception that could be attributed to the sustained entrainment of endogenous alpha-band oscillations. In Chapter 2, we tested the hypothesis that the attentional blink is strongly enhanced by alpha-band entrainment due to the suppressive role of alpha band activity in perception. Instead, we found that a similar, robust attentional blink is produced following presentation at multiple, non-alpha frequencies, and that differences in blink magnitude that vary with stream frequency can likely be attributed to previously established target-mask timing differences. In Chapter 3, we tested whether rhythmic visual stimulation with letter stimuli leads to an entrained, phase-locked fluctuation in masked target discrimination performance. Instead, we found that target performance increased monotonically with increasing frequency and propose that some previously reported benefits of rhythmic stimulation can be attributed to enhanced preparatory cortical stimulation of the visual system (i.e. “warming-up”) rather than rhythmic entrainment benefits when targets are presented at the “in-phase” moment in time. In Chapter 4, we attempted to replicate the results of two previous visual entrainment experiments and failed to find evidence to support the hypothesis that rhythmic stimulation leads to matching rhythmic fluctuations in target detection. In Chapter 5, we examined whether temporal acuity during a RSVP sequence is dependent on rhythmic entrainment by studying the role of object change on temporal acuity. Behavioural and EEG results were consistent with a local population, state-based model of temporal change detection and

inconsistent with the predictions of the rhythmic entrainment model. Thus, contrary to recent reports, we conclude that the visual system is strongly resistant to oscillatory distortions following rapid, rhythmic visual stimulation.

Across ten experiments with varied measures of visual perception, we found perception to be robustly resistant to oscillatory coupling to external visual stimulation. However, it must be acknowledged that the absence of evidence in support of behavioural entrainment is not sufficient to conclude that visual perceptual entrainment never occurs. As such, it is important to address the blind spots and limitations of the current work. Could it still be the case that rapid visual entrainment of endogenous oscillations produces perceptual consequences?

Our limitations: How the entrainment hypothesis could still be true

We could have failed to detect entrained alterations in perception due to insufficient statistical power to detect such a signal. At the time much of the current work was conceived, large behavioural effects had been attributed to entrainment in the literature. Entrainment was previous attributed to the lion's share of the attentional blink (Zauner et al., 2012), a greater than 20% change in single target detection (Mathewson et al., 2010) and a greater than 10% change in target identification (Ariga et al., 2011; Ariga & Yokosawa, 2008). Each of the experiments in the current work was designed to have sufficient statistical power to replicate or exclude effects of the magnitude proposed in the literature. When subsequent works reported more modest benefits of entrainment (de Graaf et al., 2013; Spaak et al., 2014), we designed our attempts to replicate accordingly. While the results of experiments in the current work could often statistically exclude some of the stronger extant behavioural entrainment proposals, we acknowledge our inability to fully exclude smaller effects of entrainment. In Chapter 2, we are able to reject the hypothesis that

the attentional blink is only produced when the RSVP series preceding T2 is presented at an alpha-band frequency. However, the study was not designed to detect modest differences in blink magnitude between RSVP frequencies and whether such differences could be attributed to entrainment. In Experiment 3 of Chapter 3, we increased the number of participants so as to greatly constrain the potential magnitude of a consistent cyclical, frequency-matched response in target identification following RSVP, and explain the modest differences between frequency and target delay with an alternative non-cyclical model. In Chapter 4, we had sufficient power to find significant, substantial differences between our results and the results obtained by other labs (Mathewson et al., 2012; Spaak et al., 2014), though the number of participants and trials collected were insufficient to rule out the presence of a small (<2% amplitude), cyclical difference in hit rate as reported by de Graaf and colleagues (de Graaf et al., 2013). We cannot prove the null. Nevertheless, we believe that the presented evidence for alternative, non-oscillatory accounts of changes in perception, as well as the demonstration of the absence of entrainment of a substantial magnitude, represents a meaningful contribution to our understanding of the limited role of rhythmic entrainment in perception.

We may have failed to find evidence for behavioural entrainment because the stimuli used to entrain endogenous oscillations were ineffective. In the current reported work, we used a variety of rapidly presented “entraining” stimuli to test the entrainment hypothesis. The stimuli in each of these experiments were chosen to match or resemble those used in previous experiments that reported perceptual entrainment effects. However, it remains possible that robust behavioural entrainment exists, but the chosen stimuli were ill-suited to produce the ideal resonance response. The “entrainment” stimuli used in the current study, like previous behavioural entrainment studies, primarily consisted of moderate contrast stimuli subtending less than 10° visual angle. Higher contrast or whole field stimulation would likely produce a more robust physiological response at visual cortex (Adrian & Matthews, 1934). Such stimulation was indeed used during pilot testing, and ultimately avoided due to the discomfort/disorientation experienced by participants and the

induction of strong visual afterimages. Furthermore, previous work suggested entrainment may be spatiotopically specific (Spaak et al., 2014), which made the use of wide-field stimulation less than ideal. Still, in the absence of evidence for entrainment under focal, moderate contrast conditions, it may be worthwhile for future studies to consider the use of stronger driving stimuli. All entrainment series were presented over a period of at most three seconds in a non-blocked, event-related design, with less than 40 repetitions within a given entrainment series. Some externally evoked entrainment effects may rely on changes in spike-time dependent plasticity at the synapse that would develop over longer durations, such as proposed to explain sustained aftereffects of tACS stimulation (Vossen et al., 2014; Zaehle, Rach, & Herrmann, 2010). Lastly, for all of our experimental designs, we choose to present entraining stimuli at fixed frequencies for all participants. If a tight coupling between the entrainment frequency and the endogenous frequency is required for perceptual entrainment, as suggested by previous neurophysiological and behavioural studies (Ali, Sellers, & Frohlich, 2013; de Graaf et al., 2013), entrainment at 10.3 Hz may have been less than optimal for a subset of participants. However, the vast majority of young adults have a resting occipital alpha frequency between 8 to 12 Hz and such small (+-20%) differences in frequency would be unlikely to entirely disrupt entrainment (Ali et al., 2013).

Explicit and implied models of the consequences of visual rhythmic entrainment vary depending on the stimulation parameters and the nature of the behavioural task. Some predict poor performance due to an increase in overall magnitude of the entrained endogenous oscillation (Hanslmayr et al., 2011; Zauner et al., 2012), while others focus on the cyclical variation in perception at the rate of the entrained frequency (Mathewson et al., 2012, 2010; Spaak et al., 2014). Perceptual benefits of entrainment may occur “in-phase” (Ariga & Yokosawa, 2008; Cravo, Rohenkohl, Wyart, & Nobre, 2011; Mathewson et al., 2010), “out-of-phase” (Hickok et al., 2015; Spaak et al., 2014), or anywhere in-between (de Graaf et al., 2013). Depending on the weights and phase values given to each of these predicted aspects of entrainment in response to a given design, “predicted” outcomes can change substantially, making it difficult to specify a strict *a-priori* hypothesis to detect support for a

role of entrainment. In the current work, we based our predicted entrainment outcomes on the basis of reported outcomes in previous studies or models proposed in the extant literature most closely matching the experimental task. We employed a variety of simulation and measurement approaches in order to capture a number of possible entrainment outcomes. However, we still may have missed substantial entrainment benefits if key assumptions of extant models do not hold true. For instance, our approach generally assumed consistency in the phase of perceptual entrainment across participants, which would allow us to observe cyclical fluctuations after averaging across participants. This is an assumption held by most hypotheses and reports regarding entrainment. However, if entrainment phase is grossly inconsistent across individuals, many of the experiments we conducted would fail to detect such effects. Thus, the bounding of entrainment in the current work remains restricted to the models we tested.

None of the caveats expressed above are sufficient to explain the results of Chapter 4, in which we fail to replicate the key results of Spaak et al. (2014) and Mathewson et al. (2012), both qualitatively and quantitatively. Both of our replication studies were sufficiently powered, including as many or more trials per condition as the original studies. Both used visual stimulation parameters which were intended to match as closely as possible to the original studies, and the experimental predictions were set to match the outcome of the previous experiments. To reconcile the discrepancy in outcomes, we are forced to consider more mundane concerns. For our part, this difference in outcome could relate to known design changes, such as the addition of the adaptive thresholding procedure for target contrast in Experiment 1 of Chapter 4, or the lack of eye-tracking control in Experiment 2. Even seemingly minor changes in experimental design and implementation could substantially alter the outcome of each experiment. There are also a number of unknown or irreproducible factors which could account for differences, such as subtle changes in lighting conditions or the participant population. Without reproducing behaviour consistent with entrainment, we are unable to determine which, if any, of these factors alters sensitivity to entrainment. It would be extremely useful for groups reporting entrainment effects to continue the

study of such effects to determine the conditions under which entrainment is proposed to be most robust or weak.

We must also consider that we may have erred in the coding, collection and analysis of our experiments. It is possible, and perhaps even likely, that this work contains errors that we failed to identify. This concern of systematic error is mitigated by the consistency of qualitative outcome in the current work across studies including different monitors, independently written stimulus presentation code, and varied analysis tools. However, any error could lead to false judgement of a particular paradigm. Replications conducted by independent labs will be key in determining whether our own results hold true.

Bias in the field: How the entrainment hypothesis could be false

Finally, we must consider whether the extant literature as a whole on visual entrainment is qualitatively and quantitatively inaccurate. The absence of empirical evidence supporting visual entrainment of perception in the current work stands in stark contrast to the titles of articles in the extant literature. If rhythmic behavioural entrainment is particularly sensitive to narrow boundaries in order to be observed, and both positive and negative results were published with equal frequency and conviction, one would expect that a large percentage of research conducted to test for rhythmic entrainment of perception would fail to produce an outcome consistent with entrainment. Instead, to our knowledge, there are no published articles reporting the absence of visual, frequency-matched oscillatory entrainment of behaviour in the title or abstract, though one can occasionally find such results buried within a review or article (Janson et al., 2014; VanRullen & Koch, 2003). Assuming we did not conduct uniquely unlucky or poorly designed experiments, then we must conclude that either the topic is currently unpopular and has not warranted replication or further

investigation, or there is a systematic bias in the publication of empirical results on the topic. One source of bias that has been well known for decades is the tendency toward the publication of positive (or false-positive) results, while failing to publish negative results, a phenomenon commonly referred to as "the file-drawer problem" (Rosenthal, 1979). A recent study found that while 97 of 100 selected psychology publications reported "significant" ($p < 0.05$) results, approximately 36% of studies were replicated with $p < 0.05$, and only 47% of retested effect sizes fell within the 95% confidence intervals of the original study (Open Science, 2015).

The topics of entrained oscillations and perception may be particularly susceptible to the publication of false positive findings. In a landmark paper published in 2005, John Ioannidis proposed five corollaries for determining the probability that a research finding is true (Ioannidis, 2005). These corollaries can be summarized as declaring that the research findings of a field are more likely to be false when:

1) Studies are typically conducted with smaller sample sizes
2) Published studies report smaller effect sizes
3) More relationships are tested within a single study
4) There is increased flexibility in the experimental design and selection of reported outcomes
5) The research topic is "hotter"

Arguably, the topic of oscillatory entrainment scores particularly high in each of these categories, at an intersection between psychology and neuroscience, both of which are individually poorly reproducible fields (Button et al., 2013; Open Science, 2015). A search of PubMed reveals a 22% increase in the number of publications with the key term "psychology" in the past 5 years (2010-2015) compared to the 5 years just preceding (2005-2010). Meanwhile, the number of publications with both the terms "oscillations" and "entrainment" have increased from 92 to 217 over the same

time periods, a 236% increase. As an emerging “hot” topic that relies on evidence from extant articles reporting small effect sizes, exploratory hypothesis testing leaves open a large number of potential variables of interest and several options for fitting parameters. Combining neuroimaging with behavioural data further increases the number of testable relationships. Even assuming all tested relationships are reported, few papers correct for all independent tests conducted, greatly increasing the likelihood that a false positive result will be observed. Finally, the incentives to publish in high-impact journals often result in bold, over-confident titles and abstract descriptions, often masking a lower level of evidence than presented in the body of the text. We conclude it is likely that the magnitude of the rhythmic perceptual effects of visual entrainment, if such exist, are substantially lower than suggested by extant research.

For much of the current work, we have asked a variant of the question: Does entrainment of endogenous oscillations account for a substantial amount of variance in perception under difficult, near-threshold viewing conditions? Our limited empirical answer is no. Regardless of whether or not we may have missed subtle effects of entrainment under certain conditions, it is worth asking a different question: Why does rapid, rhythmic visual stimulation seem to have little or no impact on perception through entrainment?

Fundamental roadblocks: Why doesn’t entrainment work

The proposal that the external entrainment of endogenous oscillations leads to entrainment-based changes in perception requires the following conditions to hold true:

1) Rhythmic external stimulation must lead to the predictable increase in or phase alignment of a frequency-matched oscillation

2) The externally driven, frequency-matched oscillation must reflect the alteration of an endogenous oscillation and/or be functionally equivalent to an endogenous oscillation
3) The endogenous oscillation must *cause* predictable alterations in perception

If any of these conditions are false, substantial perceptual entrainment will not occur. We now revisit some of the evidence and assumptions motivating the entrainment hypothesis and re-examine the validity of the underlying assumptions.

Condition 1: Rhythmic external stimulation must lead to the predictable increase in or phase alignment of a frequency-matched oscillation

One popular entrainment model, as addressed in Chapter 2, suggests that visual stimulation at alpha-band frequencies increases the magnitude of alpha activity in visual cortex by resonating with an endogenous alpha network (Herrmann, 2001). However, it appears increasingly unlikely that the moderate rapid rhythmic visual stimulation of most RSVP paradigms is sufficient to increase the magnitude of endogenous alpha activity. Alpha activity as measured at the scalp has long been known to *decrease* during stimulation and over the course of hundreds of milliseconds to seconds following visual stimulation (Pfurtscheller et al., 1996) and recent evidence suggests that the phase-locked response to RSVP does not compensate for this substantial alpha desynchronization (Janson et al., 2014; Mathewson et al., 2012). Another indicator of an increase in an endogenous oscillation is the maintenance of increased power after stimulation has ceased. While Spaak et al. 2014 (Spaak et al., 2014) reported modest (~0.2 dB) increases alpha power following regular vs. irregular stimulation, others have observed no such differences (Mathewson et al., 2012). As an indicator of the suppression or absence of relevant visual processing, it should not perhaps be surprising that visual stimulation may not be the most effective avenue for promoting an increase in the magnitude of alpha activity. In the light of contemporary evidence (Janson et al., 2014), it may be that focal

letter RSVP is insufficient to substantially increase alpha magnitude beyond resting-state levels in most individuals. Alternative entrainment models, as addressed in Chapters 3 through 5, propose that entrainment does not lead to increase in alpha activity, but rather that rhythmic visual stimulation phase-locks ongoing activity, without necessarily increasing the magnitude of such an oscillation (Mathewson et al., 2012; Thut, Schyns, & Gross, 2011). The phase alignment of EEG and MEG to rhythmic visual stimulation can be easily demonstrated as steady-state visual evoked potentials (SSVEPs) (Keitel, Quigley, & Ruhnau, 2014; Spaak et al., 2014), even with stimulation of moderate intensity, such as an RSVP letter stream (Janson et al., 2014; Zauner et al., 2012). Such phase locking was also apparent in during letter RSVP in Chapter 5 of the current work, particularly for the Changing condition when the letters were varied.

Condition 2: The externally driven, frequency-matched oscillation must reflect the alteration of an endogenous oscillation and/or be functionally equivalent to an endogenous oscillation

SSVEPs can occur over a wide range of frequencies (Capilla et al., 2011; Ding, Sperling, & Srinivasan, 2006; Garcia, Srinivasan, & Serences, 2013). While some studies have reported increased responses at narrow "resonant" frequencies (Ding et al., 2006; Herrmann, 2001), the increased "resonance" at particular frequencies such as alpha may simply reflect the superposition of ERP responses which have inherent response properties depending on the overall rate of stimulation (Capilla et al., 2011). In fact, Capilla and colleagues observed no difference in response between temporally jittered and non-jittered visual stimulation when accounting for such superposition, and no evidence of phase maintenance beyond the final stimulus presentation. Further, it is known that observed alpha SSVEP frequencies and topography can be distinct from an individuals' endogenous alpha frequency (Keitel et al., 2014). This overlap of endogenous alpha activity with alpha-band visually driven activity demonstrates the inability to attribute an increase in frequency-matched power at the scalp with the

entrainment of an endogenous oscillation. Even in the case of a perfect match between the frequency of visual stimulation and measured alpha frequency and topography at the scalp, superposition of endogenous and evoked activity cannot be adequately ruled out (Mazaheri & Jensen, 2006; Sauseng et al., 2007). Thus, although increases in phase-aligned alpha-band activity indicate a neural response at the rate of stimulation, there is insufficient evidence to assume any equivalence or constructive interaction with endogenous oscillations.

Condition 3: The endogenous oscillation must cause predictable alterations in perception

Finally, all perceptual entrainment models rely on the assumption that endogenous activity is inherently causally linked to perceptual outcomes. While this conjecture has recently been taken for granted regarding the alpha-band, it is worth revisiting in light of the current results as well as recent publications. It remains well established that the magnitude of occipital alpha power measured at the scalp is nearly always negatively associated with visual perceptual performance when statistically significant relationships are observed (Hanslmayr et al., 2007; Kelly, Lalor, Reilly, & Foxe, 2006; Myers et al., 2014) and that the phase of alpha and high-theta activity has been shown to be statistically related to perception of near-threshold visual stimuli (Busch et al., 2009; Mathewson et al., 2009). However, the effect sizes of alpha/perception relationships tend to be smaller (<5% change in hit rate) than would be expected for a fundamental mechanism responsible for gating perception (Jensen & Mazaheri, 2010). Yet even these modest results are subject to inflation via publication bias as discussed earlier, suggesting such effects, if existent, are likely even smaller than reported. It could be argued that the weakness of such relationships is due to the coarse spatial resolution of EEG or MEG failing to capture more robust local relationships between alpha activity and neural activity. At the level of local LFP in early visual and somatosensory areas, more substantial changes in multi- unit firing rate were observed in response to alpha phase, though still

accounting for a minority of the variance, with greatest variance explained at the lowest firing rate (i.e. idling) (Bollimunta et al., 2011; Haegens et al., 2011). Rather than focus on the small amount of variance accounted for by alpha state, we could rephrase the results of these scalp and invasive imaging experiments as supporting the statement that neuronal and perceptual processing is generally robust at all magnitudes and phases of endogenous alpha activity.

Several papers have been published recently arguing for a causal role of alpha activity on perception on the basis of perceptual response during or following rhythmic brain stimulation, such as tACS. Even discounting publication bias, tACS could be viewed as having a track record of overconfidence in demonstrating casual effects of alpha-band cortical entrainment on rhythmic perception. For instance, while the perception of phosphenes during tACS was originally reported to be due to occipital cortical excitation (Kanai, Chaieb, Antal, Walsh, & Paulus, 2008), this effect was later shown to be almost certainly due to unintended retinal stimulation rather than the direct induction of fluctuations in visual cortex (Laakso & Hirata, 2013; Schutter & Hortensius, 2010). While most subsequent studies have accounted for this issue by lowering stimulation to just below the reported phosphene threshold, retinal contributions to observed outcomes can no longer be completely discounted. There exists limited evidence that rhythmic tACS stimulation generates matching changes in perception. While one study reported phase dependent modulation of perception during alpha-band stimulation, closer examination reveals this result is based on reported phase dependent changes in accuracy in the Sham condition (Helfrich et al., 2014). While studies have shown increases in alpha power following alpha tACS stimulation (Zaehle et al., 2010), such effects were subsequently shown to likely result from long term changes in plasticity, rather than instantaneous entrainment (Vossen et al., 2014). Frequency-dependent, though not necessarily frequency-matched, state changes could also explain other recent alpha-band tACS behavioural results attributed to entrainment (Cecere et al., 2014; Müller, Vellage, Heinze, & Zaehle, 2015). While occipital alpha activity is generally associated with poorer perception, one study showed slight *improvements* in speeded perception during tACS at 6 and 10 Hz vs Sham, without any retinotopic specificity (Brignani,

Ruzzoli, Mauri, & Miniussi, 2013). This modest improvement fits with very modestly *increased* bold activity during 10 Hz tACS stimulation (Alekseichuk, Diers, Paulus, & Antal, 2015). The absence of a phasic or suppressive visual perceptual effect and the presence of a modest positive BOLD effect of 10 Hz tACS demonstrate our inability to assume direct correspondence between rhythmic stimulation and endogenous outcomes. On the other hand, rTMS applied to the parietal lobe in the alpha band has been reported to lead to rhythmic EEG aftereffects (Thut, Veniero, et al., 2011), with somewhat more conceptually consistent behavioural consequences (Jaegle & Ro, 2013; Romei, Gross, & Thut, 2010), though even these results remain mixed (Dombrowe, Juravle, Alavash, Gießing, & Hilgetag, 2015). Perhaps it is not surprising to see stronger effects reported during and following rTMS, which is caused by intense local suprathreshold firing and is far more disruptive than tACS. As with imaging experiments, we could collectively rephrase the outcome of brain stimulation experiments as supporting the statement that the vast majority of cognitive processing is neither reliant on nor disrupted by modest, induced oscillatory fluctuations in field potential.

The Big Picture

The protection of endogenous processing in the visual system *against* entrainment to external visual stimulation is likely evolutionarily useful. In the auditory system, entrainment in the theta band (4-8 Hz) is proposed to be functionally useful by assisting in the selection and tracking of human speech, which has a natural rhythm at 4-8 Hz (Henry & Obleser, 2012; Hickok et al., 2015; Luo & Poeppel, 2007). An ecological valid situation requiring the selection and tracking of alpha-band modulated visual stimuli is more difficult to surmise. To have poorer visual acuity following exposure to a particular visual frequency, or to hallucinate the continuation of a rhythmic visual object, would reflect a sub-optimal visual system design without benefit. Still, there are cases when the visual system performs sub-optimally under perceptual conditions that are extremely rare outside a

laboratory setting and thereby escape evolutionary pressure, such as the attentional blink or the retinal blind spot. Knowledge of these effects helped us gain insight into how the visual system operates under relevant, everyday conditions. In the case of rhythmic visual stimulation, it is useful to know that the brain does not allow task-irrelevant external rhythmic visual stimulation to globally override basic visual functions.

It is also particularly useful at this time to critically investigate, rather than assume, a one-to-one correspondence between putative functions of oscillatory brain activity and sensory or electrical stimulation. Various forms of entrainment are currently being used for the treatment of clinical disorders. Some treatments, such as deep brain stimulation treatment of Parkinson's disease (Deuschl et al., 2006), offer clear, unambiguous benefits leading to symptom reduction in patients. Other treatments, such as audio-visual entrainment therapy (Huang & Charyton, 2008), are currently being used in clinical practice despite questionable theoretical underpinnings and efficacy. With the surge of interest in clinical applications for sensory and transcranial brainwave entrainment (Brittain, Probert-Smith, Aziz, & Brown, 2013; Calderone, Lakatos, Butler, & Castellanos, 2014; Rafal, Smith, Krantz, Cohen, & Brennan, 1990; Ronconi, Pincham, Szűcs, & Facoetti, 2015; Thut, Schyns, et al., 2011), it is critical to understand how rhythmic stimulation affects the brain in order to promote justifiable, effective methods for basic scientific and clinical practice.

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Appendix A

Model Formulas for Chapter 3: Experiment 3

Cortical Activation Model:

$$f(PF, TD, \alpha, \beta, \delta, \gamma) = \alpha e^{\frac{\log \beta^2 - \log PF^2}{2\delta}} \times 1^{\frac{TD \times \gamma}{PF}}_{\frac{1}{2}}$$

Frequency-Matched Entrainment Model:

$$f(PF, TD, \alpha, \beta, \theta) = \alpha \cos\left(2\pi PF \times \left(\frac{1}{TD}\right) + \theta\right) \times 1^{\frac{TD \times \beta}{PF}}_{\frac{1}{2}}$$

Alpha Entrainment Model:

If *PF = 10.3*

$$f(PF, TD, \alpha, \beta, \theta) = \alpha \cos\left(2\pi PF \times \left(\frac{1}{TD}\right) + \theta\right) \times 1^{\frac{TD \times \beta}{PF}}_{\frac{1}{2}}$$

Else

$$f(PF, TD, \alpha, \beta, \theta) = 0$$

Appendix B

The answer of yes to any of the following questions excluded individuals from participation in the EEG study (Chapter 5, Experiment 2):

Do you have a neuropsychological injury?

Do you have a history of psychiatric disorder?

Do you have a history of epilepsy?

Does anyone in your immediate or distant family suffer from epilepsy?

Did you suffer from febrile seizures as an infant?

Do you have or have you ever had recurrent fainting spells?

Do you have a visual impairment that cannot be corrected with spectacles?

Do you have significant hearing loss?

Have you ever had a neurosurgical procedure (or an eye surgery?)

Are you on any currently not-prescribed or prescribed medications (besides oral contraceptives) ?

Are you currently undergoing anti - malarial treatment?

Have you drunk more than 3 units of alcohol in the last 24 hours?

Have you drunk alcohol already today?

Have you had more than one cup of coffee, or other sources of caffeine, in the last hour?

Have you used recreational drugs in the last 24 hours?

Did you have very little sleep last night?

In addition, yes to any of the following questions excluded individuals from participation in the tACS study:

Have you already participated in a TMS/TCS experiment today?

Have you participated in more that a TMS/TCS experiment in the last 6 months?

Is there any chance that you could be pregnant?

Do you currently have any of the following fitted to your body?

Heart pacemaker

Cochlear implant

Medication pump

Surgical clips